Overview

This document addresses the use of Velcade (bortezomib). Velcade is a reversible proteasome inhibitor that is used to treat multiple myeloma and other select blood dyscrasias.

The FDA approved indications for Velcade include multiple myeloma (MM) and mantle cell lymphoma. The National Comprehensive Cancer Network® (NCCN) provides additional recommendations with a category 2A level of evidence for the use of Velcade. It is recommended in the primary and subsequent treatment of Waldenström's macroglobulinemia (WM), a type of plasma cell dyscrasia. It is also recommended in the treatment of systemic light chain amyloidosis (i.e. AL amyloidosis) which is an overproduction of antibody components often associated with underlying blood disorders such as MM and WM.

Peripheral T-cell lymphomas (PTCL) are a heterogeneous and relatively uncommon group of lymphoproliferative disorders arising from mature T-cells of post-thymic origin. The prognosis for PTCL remains poor due largely to lower response rates and less durable responses to standard combination chemotherapy. Evidence in the peer-reviewed published medical literature for use of Velcade in PTCL consists of single case studies and small phase I/II clinical trials (Evens 2013; Zinzani 2007). NCCN includes a 2B recommendation for the off-label use of bortezomib as second-line therapy for non-transplant candidates.

POEMS syndrome, also known as Takatsuki syndrome or osteosclerotic myeloma, is a rare paraneoplastic syndrome that occurs in the setting of a plasma cell dyscrasia with features that include polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes. Therapeutic options for the treatment of POEMS have included use of alkylators and steroids, high-dose chemotherapy with autologous peripheral blood stem cell transplantation, lenalidomide, and bortezomib. The use of bortezomib in the treatment of POEMS syndrome has been evaluated in single and small case series; however, the benefit of bortezomib needs to be weighed against the risk of exacerbating any existing peripheral neuropathy (Dispenzieri 2017; Ishii 2013; Li 2013).

Other Uses

NCCN also recommends Velcade in the second line or subsequent treatment of adult T-cell leukemia/lymphoma; however, this recommendation was updated from a 2B to 2A recommendation in 2018 with the same underlying literature support of one small, single arm, phase 2 study (Ishitsuka 2015). NCCN also provides a 2A recommendation for Velcade in Castleman’s disease, a rare lymphoproliferative disorder. However, this recommendation does not cite literature support or appear in the discussion section of the guideline. Additional evidence regarding the use of bortezomib to treat Castleman’s disease is limited to single case studies.

Definitions and Measures

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.
When a drug is being reviewed for coverage under a member’s medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

**Velcade (bortezomib)**

Requests for Velcade (bortezomib) may be approved if the following criteria are met:

I. Individual has a diagnosis of one of the following:
   A. Multiple myeloma; **OR**
   B. One of the following non-Hodgkin lymphomas:
      1. Mantle cell lymphoma; **OR**
      2. Peripheral T-cell lymphomas (that is, peripheral T-cell lymphoma [PTCL], anaplastic large cell lymphoma [ALCL], or angioimmunoblastic T cell lymphoma [AITL]) as therapy for refractory or relapsed disease (NCCN 2B); **OR**
      3. Waldenström's macroglobulinemia/ lymphoplasmacytic lymphoma (NCCN 2A);
   **OR**
   C. Systemic light chain amyloidosis (NCCN 2A); **OR**
   D. Other rare plasma cell dyscrasias requiring treatment, including but not limited to, POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes) syndrome (Dispenzieri 2017).

Requests for Velcade (bortezomib) may not be approved for the following:

I. All other indications not included above; including but not limited to:
   A. Chronic lymphocytic lymphoma (CLL); **OR**
   B. Chronic myeloid leukemia (CML); **OR**
   C. Diffuse large B-cell lymphoma (DLBCL); **OR**
   D. Follicular lymphoma (FL); **OR**
   E. Gastric and non-gastric mucosa-associated lymphoid tissue (MALT) lymphoma; **OR**
   F. Hodgkin lymphoma (HL); **OR**
   G. Mycosis fungoides/Sézary syndrome; **OR**
   H. Myelodysplastic syndrome; **OR**
   I. Neuroendocrine tumors (for example, carcinoid or islet cell tumors); **OR**
   J. Sarcoma (for example, osteosarcoma); **OR**
   K. Solid tumors (for example, biliary tract, colorectal, head and neck, metastatic melanoma (lung), non-small cell lung cancer [NSCLC], or pancreatic carcinoma); **OR**
   L. Solitary plasmacytoma.

**Coding**

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

**HCPCS**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>J9041</td>
<td>Injection, bortezomib (Velcade), 0.1 mg</td>
</tr>
<tr>
<td>J9044</td>
<td>Injection, bortezomib, not otherwise specified, 0.1 mg [Note: code effective 01/01/2019]</td>
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**ICD-10 Diagnosis**

<table>
<thead>
<tr>
<th>Code</th>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>C83.10-C83.19</td>
<td>Mantle cell lymphoma</td>
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<tr>
<td>C84.40-C84.49</td>
<td>Peripheral T-cell lymphoma</td>
</tr>
<tr>
<td>C84.60-C84.69</td>
<td>Anaplastic large cell lymphoma, ALK-positive</td>
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<tr>
<td>C84.70-C84.79</td>
<td>Anaplastic large cell lymphoma, ALK-negative</td>
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<td>C86.2</td>
<td>Enteropathy-type (intestinal) T-cell lymphoma</td>
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<tr>
<td>C86.5</td>
<td>Angioimmunoblastic T-cell lymphoma</td>
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<tr>
<td>C88.0</td>
<td>Waldenström macroglobulinemia</td>
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<tr>
<td>C90.00-C90.02</td>
<td>Multiple myeloma</td>
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<td>D47.Z9</td>
<td>Other specified neoplasms of uncertain behavior of lymphoid, hematopoietic and related tissue</td>
</tr>
<tr>
<td>E85.81</td>
<td>Light chain (AL) amyloidosis</td>
</tr>
</tbody>
</table>
E88.09 Other disorders of plasma-protein metabolism, not elsewhere classified [when specified as POEMS syndrome]
Z85.72 Personal history of non-Hodgkin lymphomas
Z85.79 Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues

**Document History**

Revised: 05/17/2019

Document History:

**References**

   d. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma. V2.2019. Revised September 14, 2018
   e. Systemic Light Chain Amyloidosis. V1.2019. Revised October 26, 2018

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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