### Velcade (bortezomib)

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<th>Line(s) of Business:</th>
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**POLICY**

**A. INDICATIONS**

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

**FDA-Approved Indications**

- Treatment of patients with multiple myeloma
- Treatment of patients with mantle cell lymphoma

**Compendial Uses**

- Active (symptomatic) multiple myeloma
  - Primary therapy for active symptomatic myeloma or for disease relapse after 6 months following primary therapy with the same regimen in combination with dexamethasone, dexamethasone and cyclophosphamide, dexamethasone and doxorubicin, dexamethasone and lenalidomide for transplant candidates, or dexamethasone and thalidomide for transplant candidates
  - Primary therapy in combination with dexamethasone, dexamethasone and cyclophosphamide, dexamethasone and lenalidomide for nontransplant candidates
  - Maintenance therapy as monotherapy for active myeloma responding to primary therapy or for stable or responsive disease following stem cell transplant
  - Maintenance therapy as a single agent with tandem transplant for stable or responsive disease following autologous stem cell transplant
  - Therapy for previously treated myeloma for disease relapse or for progressive or refractory disease in patients who will not be treated with the same therapy as primary therapy
    - in combination with dexamethasone, dexamethasone and daratumumab, dexamethasone and cyclophosphamide, dexamethasone and lenalidomide, or with dexamethasone and bendamustine
    - VTD-PACE (bortezomib, thalidomide, dexamethasone, cisplatin, doxorubicin, cyclophosphamide, and etoposide) regimen
    - In combination with pomalidomide and dexamethasone for patients who have received at least two prior therapies, including an immunomodulatory agent and a proteasome inhibitor, and have demonstrated disease progression on or within 60 days of completion of the last therapy
- In combination with liposomal doxorubicin
- combination with elotuzumab and dexamethasone for patients who have received one to three prior therapies
- combination with panobinostat and dexamethasone for patients who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent
- Systemic light chain amyloidosis as a single agent or in combination with dexamethasone, dexamethasone and melphalan, or dexamethasone and cyclophosphamide
- Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma as a single agent, or in combination with dexamethasone, rituximab, or rituximab and dexamethasone as primary therapy or therapy or previously treated disease that does not respond to primary therapy or for progressive or relapsed disease.
- Mantle cell lymphoma used for stage I-II disease, aggressive stage II bulky, III or IV disease, or symptomatic indolent stage II bulky, III or IV disease as
  - Less aggressive induction therapy with VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone) regimen
  - Second-line therapy with or without rituximab to achieve complete response to induction therapy or for relapsed, refractory or progressive disease
  - Second line therapy with bendamustine and rituximab to achieve complete response after partial response to induction therapy or for relapsed, refractory or progressive disease.
- Castleman’s disease
  - Subsequent therapy with or without rituximab for multicentric Castleman’s disease that has progressed following treatment of relapsed/refractory or progressive disease.

B. REQUIRED DOCUMENTATION
The following information is necessary to initiate the prior authorization review:
- For members starting treatment: the patient’s treatment plan with treatment regimen including dose, frequency, length of each cycle, number of cycles, and additional therapies (e.g., other medications, radiation) must be documented.
- For members continuing treatment: relevant laboratory reports, imaging studies, and office notes to substantiate status and progression of disease

C. PRESCRIBER RESTRICTION
The medication must be prescribed by, or in conjunction with, an oncologist or hematologist.

D. INITIAL CRITERIA FOR APPROVAL
1. Systemic light chain amyloidosis
   a. Authorization of 6 months may be granted for members prescribed Velcade for the treatment of systemic light chain amyloidosis as monotherapy or in combination with ANY of the following regimens:
      i. Dexamethasone
      ii. Dexamethasone and melphalan
      iii. Dexamethasone and cyclophosphamide
2. **Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma**
   a. Authorization of 6 months may be granted for members prescribed Velcade for the treatment of Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma as monotherapy or in combination with ANY of the following regimens:
      i. Dexamethasone
      ii. Rituximab
      iii. Dexamethasone and rituximab

3. **Active (symptomatic) multiple myeloma**
   a. Member has active myeloma defined as clonal bone marrow plasma cells ≥ 10% or biopsy-proven bony or extramedullary plasmacytoma AND any one or more of the following myeloma-defining events:
      i. Serum calcium level greater than 11.0 mg/dl or > 1 mg/dl higher than the upper limit of normal
      ii. Renal insufficiency (serum creatinine greater than 2 mg/dl or creatinine clearance < 40 ml/min)
      iii. Anemia (hemoglobin level less than 10 g/dl or > 2 g/dl below lower limit of normal)
      iv. Osteolytic bone lesions on X-ray, CT or PET-CT
      v. Clonal bone marrow plasma cells ≥ 60%
      vi. Abnormal serum free light chain (FLC) ratio ≥ 100 (involved kappa) or < 0.01 (involved lambda)
      vii. More than 1 focal lesion on MRI studies > 5 mm
   b. Authorization of 6 months may be granted for members prescribed Velcade as primary therapy for the treatment of multiple myeloma in patients who are eligible for stem cell transplant in combination with ANY of the following regimens:
      i. Dexamethasone
      ii. Dexamethasone and cyclophosphamide
      iii. Dexamethasone and doxorubicin
      iv. Dexamethasone and lenalidomide
      v. Dexamethasone and thalidomide
   b. Authorization of 6 months may be granted for members prescribed Velcade as primary therapy for the treatment of multiple myeloma in patients who are NOT eligible for stem cell transplant in combination with:
      i. Dexamethasone
      ii. Dexamethasone and cyclophosphamide
      iii. Dexamethasone and lenalidomide
   c. Authorization of 6 months may be granted for members prescribed Velcade as maintenance therapy for the treatment of multiple myeloma as monotherapy
   d. Authorization of 6 months may be granted for members prescribed Velcade as therapy for the treatment of previously treated or relapsed multiple myeloma as part of ANY of the following regimens:
      i. In combination with dexamethasone
      ii. In combination with dexamethasone and daratumumab
iii. In combination with dexamethasone and cyclophosphamide
iv. In combination with dexamethasone and lenalidomide
v. In combination with dexamethasone and bendamustine
vi. In combination with dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, and etoposide (VTD-pace)
vii. In combination with dexamethasone and pomalidomide for those who have received at least 2 prior regimens including a proteasome inhibitor and an immunomodulatory agent and have demonstrated disease progression on or within 60 days of completion of the last therapy
viii. In combination with liposomal doxorubicin
ix. In combination with elotuzumab and dexamethasone for patients who have received one to three prior therapies
x. In combination with panobinostat and dexamethasone for patients who have received at least 2 prior regimens including bortezomib and an immunomodulatory agent

e. Authorization of 6 months may be granted for members prescribed Velcade as therapy for the treatment of relapsed multiple myeloma who will be receiving the same therapy as their primary chemotherapy, were transplant candidates, and the relapse occurred at least 6 months after their primary chemotherapy as part of ANY of the following regimens:
i. Dexamethasone
ii. Dexamethasone and cyclophosphamide
iii. Dexamethasone and doxorubicin
iv. Dexamethasone and lenalidomide
v. Dexamethasone and thalidomide

f. Authorization of 6 months may be granted for members prescribed Velcade as therapy for the treatment of relapsed multiple myeloma in patients who will be receiving the same therapy as their primary chemotherapy, were NOT transplant candidates, and the relapse occurred at least 6 months after their primary chemotherapy as part of ANY of the following regimens:
i. Dexamethasone
ii. Dexamethasone and cyclophosphamide
iii. Dexamethasone and lenalidomide

4. **Mantle Cell Lymphoma**
   a. Authorization of 6 months may be granted for members prescribed Velcade for induction therapy for mantle cell lymphoma as part of the VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone) regimen

   b. Authorization of 6 months may be granted for members prescribed Velcade for second-line therapy for mantle cell lymphoma with or without rituximab for relapsed, refractory, or progressive disease

5. **Castleman’s Disease**
   a. Authorization of 6 months may be granted for members prescribed Velcade for the treatment of multicentric Castleman’s disease and Velcade will be used with or without rituximab as subsequent therapy for disease that has progressed following treatment of relapsed, refractory, or progressive disease.
E. CONTINUATION OF THERAPY
1. No previous authorization/precertification:
   All members (including new members and members currently receiving treatment without prior authorization) must meet criteria for initial approval in section D.
2. Reauthorization:
   Authorization of 6 months may be granted to members who are prescribed Velcade for continuation of therapy if Velcade was previously authorized by HMSA/CVS and there is evidence of a lack of disease progression on therapy and by supplying the following information:
   a. A current oncology note documenting the patient’s response to treatment showing no progression of disease
   b. Current laboratory reports (e.g., beta-2 microglobulin, serum free light chain assay, or serum immunoglobulin) or other objective measures showing no progression of disease when compared with previous results.

F. DOSING AND ADMINISTRATION
   Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

G. ADMINISTRATIVE GUIDELINES
   Precertification is required. Please refer to the [HMSA medical policy web site](#) for the fax form.

H. IMPORTANT REMINDER
   The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

   Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

   This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA/CVS’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

I. REFERENCES
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