I. Description

Bortezomib (Velcade) is an antineoplastic agent known as a proteasome inhibitor. Proteasomes are enzymes found in cells and play an important role in regulating cell function and growth. Bortezomib blocks the activity of proteasomes. By blocking proteasomes, bortezomib disrupts processes related to the growth and survival of cancer cells. Bortezomib is an injectable and is FDA approved for the treatment of patients with multiple myeloma or mantle cell lymphoma.

II. Criteria/Guidelines

A. Bortezomib is covered (subject to Limitations and Administrative Guidelines) when recommended by a hematologist/oncologist for the following indications:

1. Multiple Myeloma
   a. Primary chemotherapy for solitary plasmacytoma that has progressed to active (symptomatic) myeloma or smoldering myeloma (asymptomatic) that has progressed to active (symptomatic) myeloma (See Appendix):
      i. In combination with dexamethasone with or without cyclophosphamide, doxorubicin, lenalidomide, or thalidomide for transplant candidates (all preferred regimens)
      ii. In combination with dexamethasone or in MPB (melphalan, prednisone, and bortezomib) regimen for nontransplant candidates (all preferred regimens)
   b. Maintenance therapy as a single agent:
      i. For active (symptomatic) myeloma responding to primary myeloma therapy
      ii. For stable or responsive disease following stem cell transplant
      iii. With second tandem transplant for stable or responsive disease following autologous stem cell transplant
   c. Therapy on or off clinical trials for disease relapse after 6 months following primary chemotherapy with the same regimen:
i. In combination with dexamethasone with or without cyclophosphamide, doxorubicin, lenalidomide, or thalidomide for transplant candidates
ii. In combination with dexamethasone or in MPB (melphalan, prednisone, and bortezomib) regimen for nontransplant candidates
d. Therapy for previously treated myeloma on or off clinical trials for disease relapse or for progressive or refractory disease:
   i. As a single agent (preferred)
   ii. In combination with dexamethasone with or without lenalidomide, cyclophosphamide, or thalidomide (all preferred regimens)
   iii. In combination with liposomal doxorubicin (preferred)
   iv. In VTD-PACE (bortezomib, dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, and etoposide) regimen (preferred)
   v. In combination with vorinostat
2. Multiple Myeloma associated with systemic light-chain amyloidosis when used in primary treatment as a single agent or in combination with dexamethasone with or without melphalan or with or without cyclophosphamide.
3. Waldenström’s Macroglobulinemia/Lymphoplasmacytic Lymphoma when used as a single agent, in combination with dexamethasone, or in combination with rituximab with or without dexamethasone as:
   a. Primary therapy
   b. Therapy for previously treated disease that does not respond to primary therapy or for progressive or relapsed disease.
5. Non-Hodgkin’s Lymphoma – Mantle Cell Lymphoma when used as:
   a. Less aggressive induction therapy with VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone) regimen
   b. Second-line therapy with or without rituximab for relapsed, refractory, or progressive disease
7. Non-Hodgkin’s Lymphoma – Primary Cutaneous CD30+ T-Cell Lymphoproliferative Disorders when used as single-agent therapy for relapsed or refractory:
   a. Primary cutaneous anaplastic large cell lymphoma (ALCL) with multifocal lesions
   b. Cutaneous ALCL with regional nodes (excludes systemic ALCL)
B. For all indications, HMSA follows NCCN level 1 or 2A and/or DrugDex level I or IIa recommendations.
C. Continuation of therapy for covered indications is covered (subject to Limitations and Administrative Guidelines) when initial therapy has been approved and the patient shows no progression of disease while on bortezomib.
*Note: Refractory is defined as no longer responding to therapy. Relapsed is defined as the reappearance of disease in the region of prior disease (recurrence) and/or in new regions (extension) after initial therapy and attainment of complete response

III. Limitations

A. Bortezomib is not covered as first-line therapy for patients with peripheral T-cell lymphoma or non-Hodgkins lymphoma.

B. Bortezomib is not covered for a patient who has had progression of disease while on bortezomib.

C. These criteria will continue to apply when bortezomib becomes available in generic form.

IV. Administrative Guidelines

A. Precertification is required for the initial six months of treatment. To precertify, please complete HMSA’s Drug Review Request and mail or fax the form as indicated with the following documentation:
   1. Clinical notes including previous treatments, if applicable.
   2. Current oncology notes
   3. Pathology reports
   4. Pertinent laboratory reports that will be used to monitor patient’s response to therapy (e.g., immunoglobulins, beta 2 microglobulin, free light chains).
   5. Imaging studies, if applicable.

B. Precertification is required for continuation of therapy for up to an additional six months. The following documentation from the medical record must be submitted:
   1. Clinical oncology notes documenting the patient’s response to therapy showing no progression of disease.
   2. Objective findings demonstrating no progression of disease (e.g., labs and imaging) when compared to previous studies.

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<th>HCPCS</th>
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<td>J9041</td>
<td>Injection, bortezomib, 0.1 mg</td>
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V. 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’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.

VI. References

3. NCCN Practice Guidelines in Oncology; Multiple Myeloma V.2.2015.
5. NCCN Drugs and Biologics Compendium; Bortezomib.
Appendix

Definition of Multiple Myeloma

Smoldering (Asymptomatic) Myeloma
Requires one or more of the following symptoms and no related organ or tissue impairment (no end organ damage, including bone lesions) or symptoms:
A. M-protein in serum
   1. IgG ≥3 g/dL,
   2. IgA >1 g/dL, OR
   3. Bence-Jones protein >1 g/24h
B. Bone marrow clonal plasma cells ≥10%

Active (Symptomatic) Myeloma
Requires one or more of the symptoms of Smoldering (Asymptomatic) Myeloma in addition to one or more of the following symptoms:
A. Calcium elevation (>11.5 mg/dL) [>2.65 mmol/L]
B. Renal insufficiency (creatinine >2 mg/dL) [177 µmol/L or more]
C. Anemia (hemoglobin <10 g/dL or 2 g/dL < normal) [<12.5 mmol/L < normal]
D. Bone disease (lytic or osteopenic)