Velcade™ (bortezomib)

Last Review Date: January 1, 2019	Number: MG.MM.PH.123

Definition

Velcade is a reversible inhibitor of the 26S proteasome, a protein complex that degrades ubiquitinated proteins. This inhibition affects cancer cells in a number of ways, including altering regulatory proteins, which control cell cycle progression and activation. Inhibition of the proteasome results in cell cycle arrest and apotosis.

Length of Authorization

Coverage will be provided for 6 months and may be renewed.

Dosing Limits

a. Max Units (per dose and over time)
- 140 billable units every 21 days

Guideline

INITIAL APPROVAL CRITERIA

Multiple Myeloma

a. The member has a diagnosis of solitary plasmacytoma, smoldering multiple myeloma, or multiple myeloma **AND**
b. Velcade (bortezomib) is being used as **ONE** of the following:
    1. Primary chemotherapy

i. In combination with dexamethasone, doxorubicin, lenalidomide, or thalidomide for transplant candidates **OR**
ii. In combination with dexamethasone or lenalidomide regimen for non-transplant candidates.

2. Relapse/Salvage chemotherapy with the same regimen for disease relapse > 6months following primary chemotherapy.
3. Relapse/Salvage chemotherapy for disease relapse or for progressive or refractory disease following primary chemotherapy as **ONE** of the following:
    i. In combination with dexamethasone (with or without daratumumab, lenalidomide, cyclophosphamide, or thalidomide) or with dexamethasone and bendamustine
    ii. In combination with liposomal doxorubicin
    iii. In VTD-PACE (bortezomib, dexamethasone, thalidomide, cisiplatin, doxorubicin, cyclophosphamide, and etoposide)regimen
    iv. In combination with panobinostat and dexamethasone for members who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent.
    v. Combination with pomalidomide and dexamethasone for members 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
    vi. Combination with elotuzumab and dexamethasone for members who have received one to three prior therapies.
4. Maintenance therapy as a single agent following response to primary myeloma therapy or in stable disease following stem cell transplant.

Non-Hodgkin's Lymphoma (NHL)

a. The member has a diagnosis of mantle cell lymphoma, **AND**
b. Velcade (bortezomib) is being used as a single agent as second line therapy for relapsed, refractory, or progressive disease or as less aggressive induction therapy with VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone) regimen.

Limitations:

- Velcade (bortezomib) is being used after disease progression with the same regimen.
- Dosing exceeds single dose limit of Velcade (bortezomib) 1.6 mg/m2.
- Maintenance dosing exceeds 6.4 mg/m2 every 35 day cycle or 1.3 mg/m2 every 2 weeks.
- Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

RENEWAL CRITERIA

- Patient continues to meet the criteria identified in section III; **AND**
- Tumor response with stabilization of disease or decrease in size of tumor or tumor spread; **AND**

- Absence of unacceptable toxicity from the drug

Dosage/Administration

Dosing	
Multiple Myeloma	Initial therapy: in combination with melphalan and prednisone: 1.3 mg/m2 IV bolus on days 1, 4, 8, 11, 22, 25, 29, and 32 for Cycles 1-4 followed by a rest for 10 days. For Cycles 5-9, Velcade (bortezomib) is administered weekly on days 1, 8, 22, and29 followed by a rest. The regimen is a total of nine six week treatment cycles. Relapse: 1.3mg/m2/dose given as IV bolus twice weekly for 2 weeks (i.e. on days 1,4, 8, and 11) followed by a 10-day rest; each cycle is 21 days. Consecutive doses should be administered at least 72 hours apart. For extended therapy or more than8 cycles, either a weekly schedule (once a week for 4 weeks on days 1, 8, 15, and22) every 35 day cycle or 1.3 mg/m2 every 2 weeks may be used for maintenance.
Mantle Cell Lymphoma	Relapsed: 1.3mg/m2/dose given as IV bolus twice weekly for 2 weeks (i.e. on days1, 4, 8, and 11) followed by a 10-day rest; each cycle is 21 days. Consecutive doses should be administered at least 72 hours apart. For extended therapy or more than8 cycles, either the standard schedule or a weekly schedule (once a week for 4weeks on days 1, 8, 15, and 22) followed by a 13 day rest period may be used for maintenance.
Weekly bortezomib dosing: Guidelines for weekly dosing varies in the literature. Dose range include 1.3 mg/m2 to 1.6 mg/m2 weekly intravenous administration (please see reference section for further details).	
Dosing Adjustments: 1. Renal impairment: Dosage adjustments are not required. 2. Mild hepatic impairment (bilirubin ≤1 times ULN and AST >UNL or bilirubin >1-1.5 times ULN): No initial dose adjustment required. 3. Moderate (bilirubin >1.5-3 times ULN) to severe hepatic impairment (bilirubin >3 times ULN): Reduce initial dose to 0.7 mg/m2 in the first cycle. May consider dose escalation to 1mg/m2 or further dose reduction to 0.5 mg/m2 in subsequent cycles based on member tolerance. 4. Hematologic toxicities: Interrupt and hold Velcade (bortezomib) therapy for grade 4hematologic toxicities; re-institute once the toxicity has resolved at a 25% reduced dose. 5. Non-hematologic toxicities- grade 3: Interrupt and hold Velcade (bortezomib) therapy for grade 3 non-hematologic toxicities (excluding neuropathy); re-institute once the toxicity has resolved at a 25% reduced dose. 6. Central nervous system toxicities: Decrease Velcade (bortezomib) to 1 mg/m2 if grade 1with pain or grade 2 peripheral neuropathy occurs; hold therapy until toxicity resolves and re-institute at 0.7 mg/m2/WEEK if grade 2 with pain or grade 3 peripheral	

neuropathy occurs; discontinue Velcade (bortezomib) therapy if grade 4 peripheral neuropathy occurs.

Authorization

Applicable Procedure Codes

J9041	Injection, Bortezomib, 0.1mg billable unit

Applicable NDC's

63020-0049-xx	Velcade single-use vial, 3.5mg powder for injection

Applicable Diagnosis Codes

ICD-10	ICD-10 Description
C83.00	Small cell B-cell lymphoma, unspecified site
C83.01	Small cell B-cell lymphoma, lymph nodes of head, face and neck
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.03	small cell B-cell lymphoma, intra-abdominal lymph nodes
C83.04	Small cell B-cell lymphoma, lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma, intrapelvic lymph nodes
C83.07	Small cell B-cell lymphoma, spleen
C83.08	Small cell B-cell lymphoma, lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma, extranodal and solid organ sites
C83.10	Mantle cell lymphoma, unspecified site
C83.11	Mantle cell lymphoma, lymph nodes of head, face and neck
C83.12	Mantle cell lymphoma, intrathoracic lymph nodes
C83.13	Mantle cell lymphoma, intra-abdominal lymph nodes
C83.14	Mantle cell lymphoma, lymph nodes of axilla and upper limb
C83.15	Mantle cell lymphoma, lymph nodes of inguinal region and lower limb
C83.16	Mantle cell lymphoma, intrapelvic lymph nodes
C83.17	Mantle cell lymphoma, spleen
C83.18	Mantle cell lymphoma, lymph nodes of multiple sites
C83.19	Mantle cell lymphoma, extranodal and solid organ sites
C86.6	Primary cutaneous CD30-positive T-cell proliferations
C88.0	Waldenstrom macroglobulinemia
C90.00	Multiple myeloma not having achieved remission
C90.01	Multiple myeloma in remission
C90.02	Multiple myeloma, in relapse
C90.10	Plasma cell leukemia not having achieved remission
C90.11	Plasma cell leukemia in remission
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having achieved remission

C90.21	Extramedullary plasmacytoma in remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission
C90.31	Solitary plasmacytoma in remission
C90.32	Solitary plasmacytoma in relapse
C91.50	Adult T-cell lymphoma/leukemia (HTLV-1-associated) not having achieved remission
C91.52	Adult T-cell lymphoma/leukemia (HTLV-1-associated), in relapse
D36.0	Benign neoplasm of lymph nodes
D47.Z2	Castleman disease
E85.9	Amyloidosis, unspecified
R59.0	Localized enlarged lymph nodes
R59.1	Generalized enlarged lymph nodes
R59.9	Enlarged lymph nodes, unspecified
Z85.72	Personal history of non-Hodgkin lymphomas
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues

References

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