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Subject: Bortezomib Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Bortezomib (Velcade) is a small molecule, dipeptidyl boronic acid proteasome inhibitor. The 26S proteasome degrades ubiquitinated proteins and regulates the intracellular concentration of specific cell proteins and maintains cellular homeostasis. This disruption of homeostasis can lead to cell death. The first bortezomib product, Velcade, was approved by the US Food and Drug Administration (FDA) in May 2003 for treatment of persons with multiple myeloma (MM) who received at least two prior therapies and have demonstrated progression of the disease on the last therapy. It was the first proteasome inhibitor to be approved for MM, and over time it became a standard of care in MM combination drug regimens. Since initial approval, the use of bortezomib in other MM settings (e.g., primary therapy, maintenance therapy) is supported by referenced compendia, including National Comprehensive Cancer Network (NCCN). The FDA-approved indication was expanded to treatment of MM patients who have received at least one prior therapy in May 2005, and then to first-line treatment of MM in June 2008. In December 2006, the FDA granted approval for treatment of refractory or recurrent mantle cell lymphoma (MCL), a rare form of B-cell non-Hodgkin's lymphoma (NHL). The indication was expanded to first-line treatment of MCL in October 2014.

In November 2017 the FDA approved an additional bortezomib product (manufactured by Fresenius Kabi). The product is not a true generic to Velcade since it was approved via a new drug application

(NDA). As such, there are differences in the FDA-approved indications (i.e., Velcade is approved for first-line use in MCL while bortezomib is approved for second-line use in MCL); the approved routes of administration (i.e., Velcade is approved for both IV and subcutaneous use while bortezomib is only approved for IV use; and the product formulations (i.e., Velcade contains mannitol while bortezomib contains glycine). In October 2019 another bortezomib product (manufactured by Dr. Reddy's Labs) was approve via an NDA. Its more limited labeling is similar to that of the Fresenius Kabi product, except the Dr. Reddy's product's inactive ingredients are different (contains citric acid and tromethamine). In May 2022, the FDA granted effective approval to ANDAs for eight generic versions of Takeda's Velcade. The ANDA products are approved in the form of single-use vials containing 3.5 mg bortezomib for IV or subcutaneous administration. The FDA considers these newly approved ANDA products to be therapeutically equivalent (AP-rated) to Velcade.

In addition to use in MM and MCL, the NCCN guidelines support bortezomib therapy (with a category 1 or 2A recommendation) for treatment of adult and pediatric acute lymphoblastic leukemia (ALL), adult T-cell leukemia/lymphoma, Kaposi sarcoma, multicentric Castleman's disease, pediatric Hodgkin lymphoma, POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome, systemic light chain amyloidosis, and Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma.

POSITION STATEMENT:

Initiation of bortezomib injection meets the definition of **medical necessity** when **ALL** of the following criteria are met ("1", "2", and "3"):

1. Bortezomib is used for **ANY** indication listed in Table 1, and **ALL** indication-specific criteria are met.
2. Bortezomib will **NOT** be used in combination with another proteasome inhibitor [e.g., carfilzomib (Kyprolis) or ixazomib (Ninlaro)].
3. The dosage of bortezomib does not exceed **EITHER** of the following:
    a. 1.3 mg/m^2 twice weekly for 14 days (4 doses) of a 21-day cycle (e.g., days 1, 4, 8, and 11)
    b. 1.6 mg/m^2 once weekly for 28 days (4 doses) of a 28-day or 35-day cycle (e.g., days 1, 8, 15, and 22)

Table 1

Indications and Specific Criteria	
Indication	**Criteria**
Acute Lymphoblastic Leukemia (ALL)	**ALL** of the following ("1", "2", and "3"): 1. Member has Philadelphia chromosome-negative (Ph-) T-cell lineage ALL 2. Member has relapsed/refractory disease 3. Bortezomib with be used in combination with chemotherapy

Adult T-Cell Leukemia/Lymphoma (ATLL)	**ALL** of the following ("1", "2", and "3"): 1. Bortezomib will be used as second-line or later therapy for relapsed or refractory disease 2. Member has the acute or lymphoma disease subtype (as opposed to the chronic/smoldering disease subtype) 3. Bortezomib will be used as monotherapy
Antibody-mediated transplant rejection	**BOTH** of the following ("1" and "2"): 1. Member has previously received a heart, liver, or lung transplant 2. Member is refractory to first-line therapy (such as high-dose steroids, plasmapheresis, intravenous immunoglobulin, and/or rituximab)
Desensitization therapy prior to solid-organ transplantation	**BOTH** of the following ("1" and "2"): 1. Member is highly sensitized as determined by a calculated panel reactive antibody (cPRA) of 50% or greater 2. Bortezomib will be used in combination with plasmapheresis
Kaposi sarcoma	**ALL** of the following ("1", "2", and "3"): 1. Member has relapsed/refractory advanced cutaneous, oral, visceral, or nodal disease 2. Member's disease has progressed on or not responded to first-line systemic therapy, **AND** has progressed on alternate first-line systemic therapy 3. Treatment will be given either alone (members without HIV) or in combination with antiretroviral therapy (ART) (members with HIV
Lymphoplasmacytic lymphoma	**ANY** of the following regimens will be used: • Bortezomib monotherapy • Bortezomib + dexamethasone • Bortezomib + rituximab • Bortezomib + rituximab + dexamethasone
Mantle cell lymphoma (MCL)	Bortezomib will be used in **EITHER** of the following settings ("1" or "2"): 1. Less aggressive induction therapy as part of the VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone) regimen 2. Second-line or later therapy for relapsed, refractory, or progressive disease, **AND ANY** of the following regimens will be used: a. Bortezomib monotherapy

	b. Bortezomib + rituximab c. VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone) regimen [only if not previously given]
Multicentric Castleman's disease (CD)	**BOTH** of the following ("1" and "2"): 1. Bortezomib will be used as subsequent therapy for disease that has progressed following treatment of relapsed/refractory or progressive disease (i.e., third-line or later treatment) 2. Bortezomib will be used as either monotherapy or in combination with rituximab
Multiple myeloma (MM)	Member has **symptomatic** multiple myeloma [as opposed to smoldering myeloma (asymptomatic)]
Pediatric acute lymphoblastic leukemia (ALL)	**BOTH** of the following ("1" and "2"): 1. Member has relapsed/refractory disease 2. **ANY** of the following ("a", "b", or "c"): a. Member has T-cell lineage ALL (T-ALL), and treatment will be used as a component of a bortezomib-containing regimen (for example: bortezomib, vincristine, doxorubicin, pegaspargase, and prednisone or dexamethasone) b. Member has Ph-negative B-cell lineage ALL (B-ALL) c. Member has Ph-positive B-ALL, and treatment will be used in in combination with dasatinib or imatinib as a component of COG AALL07P1 regimen
Pediatric Hodgkin lymphoma	**BOTH** of the following ("1" and "2"): 1. Member has relapsed/refractory disease 2. Bortezomib will be used in combination with both ifosfamide and vinorelbine
POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome	Treatment will be used in combination with dexamethasone
Systemic light chain amyloidosis (SLCA)	**BOTH** of the following ("1"and "2"): 1. The diagnosis has been confirmed by the presence of amyloid deposits in tissue **AND** the deposits are composed of light chains 2. One of the following regimens will be used ("a" to "f"): a. Bortezomib monotherapy b. Bortezomib + dexamethasone

	c. Bortezomib + cyclophosphamide + dexamethasone d. Bortezomib + lenalidomide + dexamethasone e. Bortezomib + melphalan + dexamethasone f. Bortezomib + daratumumab or daratumumab-hyaluronidase + cyclophosphamide + dexamethasone
Waldenström's macroglobulinemia	**ANY** of the following regimens will be used: • Bortezomib monotherapy • Bortezomib + dexamethasone • Bortezomib + rituximab • Bortezomib + rituximab + dexamethasone
Other FDA-approved or NCCN supported diagnosis (not previously listed above and not an orphan indication)	**EITHER** of the following ("1" or "2"): 1. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert) 2. Indication **AND** usage are recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation
Approval duration: 6 months (except for antibody-mediated transplant rejection – approve for 3 months; and desensitization therapy prior to solid-organ transplantation - approve for 1 month)	

Continuation of bortezomib injection **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "4"):

1. Authorization or reauthorization for bortezomib has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of any indications listed in Table 1 (except for antibody-mediated transplant rejection, and desensitization therapy prior to solid-organ transplantation – use initiation criteria), **OR** the member previously met **ALL** indication-specific initiation criteria
2. Member has not had disease progression during bortezomib treatment
3. Bortezomib will **NOT** be used in combination with another proteasome inhibitor [e.g., carfilzomib (Kyprolis) or ixazomib (Ninlaro)].
4. The dosage of bortezomib does not exceed **EITHER** of the following:
    a. 1.3 mg/m^2 twice weekly for 14 days (4 doses) of a 21-day cycle (e.g., days 1, 4, 8, and 11)
    b. 1.6 mg/m^2 once weekly for 28 days (4 doses) of a 28-day or 35-day cycle (e.g., days 1, 8, 15, and 22)

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved:

- Velcade (and AP-rated generics) - indicated for the treatment of adult patients with multiple myeloma and the treatment of adult patients with mantle cell lymphoma. The recommended dose is 1.3 mg/m^2 either as a 3 to 5 second bolus intravenous injection (1 mg/mL) or as a subcutaneous injection (2.5 mg/mL). The frequency of administration is dependent on the indication for therapy. See the package insert for specific dosage recommendations.
- Bortezomib (Fresenius Kabi) and Bortezomib (Dr. Reddy's) - indicated for the treatment of adult patients with multiple myeloma and the treatment of adult patients with mantle cell lymphoma who have received at least 1 prior therapy. The recommended dose is 1.3 mg/m^2 administered as a 3 to 5 second bolus intravenous injection (1 mg/mL). For intravenous use only. The frequency of administration is dependent on the indication for therapy. See the package insert for specific dosage recommendations.

Dosage Modifications: See the package insert for specific dosage adjustments based on toxicity. No dosage adjustment is needed in patients with renal impairment. The exposure of bortezomib is increased in patients with moderate (bilirubin ≥1.5 to 3-times the ULN) and severe (bilirubin >3-times the ULN) hepatic impairment, and the starting dose should be reduced.

Drug Availability:

- Velcade (and AP-rated generics) are supplied as a single-use vial containing 3.5 mg of bortezomib as lyophilized powder. Each route of administration (i.e., IV or SQ) has a different reconstitution concentration and caution should be used when calculating the volume to be administered.
- Bortezomib (Fresenius Kabi) is supplied in a single-dose 10 mL vial for reconstitution containing 3.5 mg of bortezomib as a white to off-white cake or (after reconstitution the solution is clear and colorless).
- Bortezomib (Dr. Reddy's) is supplied in a single-dose 10 mL vial for reconstitution containing 3.5 mg of bortezomib as a white to off-white cake or powder (after reconstitution the solution is clear and colorless).

PRECAUTIONS:

Contraindications:

- **Velcade** (and AP-rated generics) - Patients with hypersensitivity (not including local reactions) to bortezomib, boron, or mannitol.
- **Bortezomib (Fresenius Kabi)** - Patients with hypersensitivity (not including local reactions) to bortezomib, boron, boric acid or glycine

- **Bortezomib (Dr. Reddy's) -** Patients with hypersensitivity (not including local reactions) to bortezomib or boron.
- **All products** - Intrathecal administration is contraindicated. Fatal events have occurred with intrathecal administration.

Warnings/Precautions:

- **Cardiac toxicity**: worsening of and development of cardiac failure has occurred. Closely monitor persons with existing disease or risk factors for heart disease.
- **Hepatic toxicity**: Acute liver failure has been reported in persons receiving multiple concurrent medications and with serious underlying medical conditions. Monitor hepatic enzymes during treatment.
- **Thrombotic Microangiopathy**: Monitor for signs and symptoms. Discontinue bortezomib if suspected.
- **Hypotension**: use caution when treating members prescribed antihypertensive medications, with a history of syncope, or with dehydration as this can result in increased risk of orthostatic and postural hypotension.
- **Pulmonary toxicity**: acute respiratory syndromes have occurred; monitor closely for new or worsening symptoms.
- **Gastrointestinal toxicity**: nausea, diarrhea, constipation and vomiting may require use of antiemetic and antidiarrheal medications or fluid replacement.
- **Peripheral neuropathy**: new onset or exacerbation of pre-existing peripheral neuropathy may occur; managed with dose modification or discontinuation.
- **Posterior Reversible Encephalopathy Syndrome (PRES)**: consider MRI imaging for onset of visual or neurological symptoms; discontinue bortezomib therapy in persons developing PRES.
- **Thrombocytopenia and neutropenia**: monitor complete blood counts regularly throughout treatment.
- **Tumor lysis syndrome may occur**. Closely monitor members with a high tumor burden.
- **Embryo-fetal Toxicity**: may cause embryo-fetal harm. Women should avoid becoming pregnant while being treated with bortezomib. Advise females and males of reproductive potential that they must use contraception during treatment with bortezomib and for 2 months following treatment.
- **Diabetes**: patients with diabetes may require close monitoring of blood glucose and adjustment of anti-diabetic medication.
- **Drug interactions**: co-administration with strong CYP3A4 inhibitors can increase bortezomib exposure; closely monitor. Co-administration with strong CYP3A4 inducers can decrease bortezomib exposure; avoid concomitant use.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding:

J9041	Injection, bortezomib, 0.1 mg
J9046	Injection, bortezomib, (Dr. Reddy's), not therapeutically equivalent to J9041, 0.1 mg
J9048	Injection, bortezomib (Fresenius Kabi), not therapeutically equivalent to J9041, 0.1 mg
J9049	Injection, bortezomib (Hospira), not therapeutically equivalent to J9041, 0.1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity:

B10.89	Other human herpesvirus infection [for Castleman disease only]
C46.0 – C46.9	Kaposi's sarcoma
C81.00 – C81.99	Hodgkin lymphoma
C83.10 – C83.19	Mantle cell lymphoma
C83.50 – C83.59	Lymphoblastic (diffuse) lymphoma
C88.0	Waldenstrom macroglobulinemia
C90.00 – C90.02	Multiple myeloma
C90.10 – C90.12	Plasma cell leukemia
C90.20 – C90.22	Extramedullary plasmacytoma
C90.30 - C90.32	Solitary plasmacytoma
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.02	Acute lymphoblastic leukemia, 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
D47.Z2	Castleman disease
D47.9	Neoplasm of uncertain behavior of lymphoid, hematopoietic and related tissue, unspecified [for POEMS syndrome only]
E31.9	Polyglandular dysfunction, unspecified [for POEMS syndrome only]
E85.81	Light chain (AL) amyloidosis
E85.89	Other amyloidosis
E85.9	Amyloidosis, unspecified
G62.9	Polyneuropathy, unspecified [for POEMS syndrome only]
G90.9	Disorder of the autonomic nervous system, unspecified [for POEMS syndrome only]
L98.9	Disorder of the skin and subcutaneous tissue, unspecified [for POEMS syndrome only]
T86.21	Heart transplant rejection
T86.31	Heart-lung transplant rejection
T86.41	Liver transplant rejection

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) or Local Coverage Determination (LCD) were found at the time of the last guideline revised date. The LCD, Bortezomib (Velcade) (L33273), was retired effective 11/15/19.

DEFINITIONS:

Heavy chain – the larger component of an immunoglobulin. There are five types: IgG, IgA, IgM, IgD, and IgE.

Immunoglobulins (a.k.a., antibodies) – proteins made by normal plasma cells that have an important role in fighting infection as part of the humoral immune response. Antibodies are composed of two heavy chains and two light chains that form a larger complex. Each plasma cell produces only one type of heavy chain and one type of light chain.

Light chain – the smaller component of an immunoglobulin. There are two types: kappa and lambda.

Myeloma Protein (M-Protein) – a nonfunctional immunoglobulin protein or protein fragment produced by malignant plasma cells (or myeloma cells). Since myeloma cells are monoclonal, the M-proteins for a given patient are structurally identical. Both portions of an immunoglobulin (the heavy chain and light chain) can be found in the serum, while only light chains can be found in the urine.

Plasma cell - a fully differentiated B lymphocyte (a type of white blood cell) that is specialized for immunoglobulin production and is found primarily in bone marrow.

Primary refractory MM - patients who never achieve at least a MR to initial induction therapy and progress while on therapy

Progressive MM - at least a 25% increase from nadir in the serum M-protein (absolute increase must be ≥0.5 g/dL) or urine M-protein (absolute increase must be ≥200mg/24 hours), or in the difference between involved and uninvolved serum-free light-chain (FLC) levels (with an abnormal FLC ratio and FLC difference >100 mg/L).

Relapsed and refractory MM - patients who never achieve at least a MR or who progress within 60 days of their last therapy

Serum Protein Electrophoresis (SPEP) – a test that detects and quantifies the amount of M-protein in the serum. An serum M-protein of greater than 30 g/L is consistent with a diagnosis of MM.

Smoldering (Asymptomatic) myeloma: defined as M-protein in serum of 30 g/dL or more and/or bone marrow clonal plasma cells of 10% or more, but no related organ or tissue impairment (no end organ damage, including bone lesions) or symptoms.

RELATED GUIDELINES:

Allogeneic Bone Marrow and Stem Cell Transplantation, 02-38240-01

Belantamab Mafodotin-blmf (Blenrep), 09-J3000-80
Carfilzomib (Kyprolis) IV, 09-J1000-81
Chimeric Antigen Receptor (CAR) T-Cell Therapies, 09-J3000-94
Daratumumab (Darzalex) Infusion and Daratumumab-Hyaluronidase-fihj (Darzalex Faspro) Injection, 09-J2000-49
Doxorubicin HCl Liposome (Doxil) IV, 09-J0000-91
Elotuzumab (Empliciti) IV, 09-J2000-50
Isatuximab (Sarclisa) Injection, 09-J3000-67
Ixazomib (Ninlaro), 09-J2000-51
Oral Oncology Medications, 09-J3000-65
Thalidomide (Thalomid) Capsules, 09-J1000-56

OTHER:

None.

REFERENCES:

1. Baradaran H, Dashti-Khavidaki S, Taher M, et al. Antibody-mediated rejection in adult liver transplant recipients: a case series and literature review. J Clin Pharmacol 2022; 62(2):254-271.
2. Bortezomib (bortezomib injection, powder, lyophilized, for solution) [package insert]. Dr. Reddy's Laboratories Inc. Lake Zurich (IL): October 2019.
3. Bortezomib (bortezomib injection, powder, lyophilized, solution) [package insert]. Fresenius Kabi USA. Lake Zurich (IL): March 2022.
4. Charlton M, Levitsky J, Aqel B, et al. International Liver Transplantation Society consensus statement on immunosuppression in liver transplant recipients. Transplantation 2018; 102(5):727-743
5. Chih S, McDonald M, Dipchand A, et al. Canadian Cardiovascular Society/Canadian Cardiac Transplant Network position statement on heart transplantation: patient eligibility, selection, and post-transplantation care. Can J Cardiol 2020; 36(3):335-356.
6. Clinical Pharmacology powered by ClinicalKey [Internet]. Tampa, FL: Elsevier.; 2022. https://www.clinicalkey.com/pharmacology/. Accessed 5/29/22.
7. Du XL, Chen Q. Recent advancements of bortezomib in acute lymphocytic leukemia treatment. Acta Haematol. 2013;129(4):207-14.
8. Eskandary F, Regele H, Baumann L, et al. A randomized trial of bortezomib in late antibody-mediated kidney transplant rejection. J Am Soc Nephrol 2018; 29(2):591-605
9. Fowler N, Kahl BS, Lee P, et al. Bortezomib, bendamustine, and rituximab in patients with relapsed or refractory follicular lymphoma: the phase II VERTICAL study. J Clin Oncol. 2011 Sep 1;29(25):3389-95.
10. Goy A, Bernstein SH, Kahl BS, et al. Bortezomib in patients with relapsed or refractory mantle cell lymphoma: updated time-to-event analyses of the multicenter phase 2 PINNACLE study. Ann Oncol. 2009 Mar;20(3):520-5.
11. Kastritis E, Wechalekar AD, Dimopoulos MA, et al. Bortezomib with or without dexamethasone in primary systemic (light chain) amyloidosis. J Clin Oncol. 2010 Feb 20;28(6):1031-7.
12. Micromedex Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 5/29/22.

13. National Comprehensive Cancer Network. Cancer Guidelines. Cancer Guidelines and Drugs and Biologics Compendium. Accessed 5/29/22.
14. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 1.2022 – April 4, 2022. Acute Lymphoblastic Leukemia. Available at https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed 5/30/22
15. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 3.2022 – April 25, 2022. B-cell Lymphomas. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed 5/30/22.
16. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 1.2022 – February 3, 2022. Kaposi Sarcoma. Available at https://www.nccn.org/professionals/physician_gls/pdf/kaposi.pdf. Accessed 5/30/22.
17. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 5.2022 – March 9, 2022. Multiple Myeloma. Available at http://www.nccn.org/professionals/physician_gls/PDF/myeloma.pdf. Accessed 5/30/22.
18. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 1.2022 – October 1, 2021. Pediatric Acute Lymphoblastic Leukemia. Available at https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed 5/30/22.
19. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 1.2022 – April 8, 2022. Pediatric Hodgkin Lymphoma. Available at https://www.nccn.org/professionals/physician_gls/pdf/ped_hodgkin.pdf. Accessed 5/30/22.
20. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 1.2022 – January 26, 2022. Primary Cutaneous Lymphomas. Available at https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed 5/30/22.
21. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 1.2022 – June 29, 2021. Systemic Light Chain Amyloidosis. Available at http://www.nccn.org/professionals/physician_gls/pdf/amyloidosis.pdf. Accessed 5/30/22.
22. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 2.2022 – March 7, 2022. T-cell Lymphomas. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed 5/30/22.
23. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 3.2022 – May 2, 2022. Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma. Available at http://www.nccn.org/professionals/physician_gls/PDF/waldenstroms.pdf. Accessed 5/30/22.
24. Neuhaus K, Hohlfelder B, Bollinger J, et al. Antibody-Mediated Rejection Management Following Lung Transplantation. Ann Pharmacother. 2022 Jan;56(1):60-64. Epub 2021 Apr 26.
25. Paterno F, Shiller M, Tillery G, et al. Bortezomib for acute antibody-mediated rejection in liver transplantation. Am J Transplant 2012; 12(9):2526-2531.
26. Reeder CB, Reece DE, Kukreti V, et al. Once- versus twice-weekly bortezomib induction therapy with CyBorD in newly diagnosed multiple myeloma. Blood. 2010 Apr 22;115(16):3416-7.
27. Robak T, Huang H, Jin J, et al. Bortezomib-based therapy for newly diagnosed mantle-cell lymphoma. N Engl J Med. 2015 Mar 5;372(10):944-53.
28. Treon SP, Ioakimidis L, Soumerai JD, et al. Primary therapy of Waldenström macroglobulinemia with bortezomib, dexamethasone and rituximab: WMCTG clinical trial 05-180. J Clin Oncol 2009;27(23):3830-3835.
29. Velcade (bortezomib) [package insert]. Millennium Pharmaceuticals, Inc. Cambridge (MA): November 2021.

30. Wan SS, Ying TD, Wyburn K, et al. The Treatment of Antibody-Mediated Rejection in Kidney Transplantation: An Updated Systematic Review and Meta-Analysis. Transplantation. 2018 Apr;102(4):557-568.
31. Zinzani PL, Khuageva NK, Wang H, et al. Bortezomib plus rituximab versus rituximab in patients with high-risk, relapsed, rituximab-naïve or rituximab-sensitive follicular lymphoma: subgroup analysis of a randomized phase 3 trial. Hematol Oncol. 2012 Oct 22; 5:67.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 06/08/22.

GUIDELINE UPDATE INFORMATION:

04/15/09	New Medical Coverage Guideline.
10/15/09	Revision; consisting of clarifying dosage and updating coding.
07/15/10	Review and revision; consisting of updating references.
08/01/10	Revision; consisting of updating coding.
02/01/11	Revision; consisting of updating coding.
02/15/11	Revision; consisting of adding ICD-10 codes.
07/15/11	Review and revision to guideline; consisting of updating coding and references.
07/15/12	Review and revision to guideline; consisting of updating coding, references and exceptions.
12/15/12	Revision to guideline; consisting of updating coding.
07/15/13	Review and revision to guideline; consisting of revising position statement to include updated NCCN category 1 and 2A recommendations; reformatting/revising dosage/administration, precautions, program exceptions, and description section; updating references and coding.
12/15/13	Revision to guideline; consisting of revising medical necessity criteria for coverage of mantle cell lymphoma.
07/15/14	Review and revision to guideline; consisting of revising position statement, updating references and coding.
12/15/14	Revision to guideline; consisting of position statement, dosing/administration.
07/15/15	Review and revision to guideline; consisting of updating description, position statement, dosage/administration, precautions, coding/billing, and references.
10/01/15	Revision consisting of update to Program Exceptions section.
11/01/15	Revision: ICD-9 Codes deleted.
07/15/16	Review and revision to guideline consisting of updating position statement, billing/coding information, definitions, related guidelines, and references.
10/01/16	Revision: ICD-10 code updates.
02/16/17	Revision: Update to Position Statement.
07/15/17	Review and revision to guidelines consisting of updating the description section, position statement, and references.

03/15/18	Revision to guidelines consisting of updating description, position statement, dosage/administration, precautions, coding/billing, and references based on a newly approved bortezomib product manufactured by Fresenius Kabi.
07/15/18	Review and revision to guidelines consisting of updating the description section, position statement, billing/coding information, and references.
01/01/19	Revision: HCPCS code updates. Added J9044 and removed J9999. Modified J9041 description.
07/15/19	Review and revision to guidelines consisting of updating the description section, position statement, billing/coding information, and references.
07/15/20	Review and revision to guidelines consisting of updating the description section, position statement, dosage/administration, precautions, billing/coding information, and references.
07/15/21	Review and revision to guidelines consisting of updating the description section, position statement, billing/coding information, related guidelines, and references.
07/15/22	Review and revision to guidelines consisting of updating the description section, position statement, billing/coding information, and references.
01/01/23	Revision: Added HCPCS codes J9046, J9048, and J9049, and deleted code J9044.
07/01/23	Policy archived and retired.