09-J1000-53

Original Effective Date: 01/01/12

Reviewed: 08/13/25

Revised: 07/15/26

Subject: Brentuximab (Adcetris®) 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.

Position Statement	Dosage/ Administration	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Brentuximab vedotin (Adcetris®) is an antibody-drug conjugate comprising an anti-CD30 monoclonal antibody and the potent antimicrotubule agent, monomethyl auristatin E (MMAE). The two are attached by a dipeptide link that is stable in plasma but is cleaved by intracellular lysosomal proteases; once inside the CD30-positive tumor cell, MMAE is released and ultimately results in cell cycle arrest and apoptosis. Brentuximab was approved by the US Food and Drug Administration (FDA) in August 2011 for treatment of patients with classical Hodgkin lymphoma (CHL) after failure of autologous hematopoietic stem cell transplantation (auto-HSCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates, and for systemic anaplastic large-cell lymphoma (ALCL) after failure of at least one prior multi-agent chemotherapy regimen. In August 2015, the FDA approved brentuximab for the treatment of patients with classical Hodgkin lymphoma at high risk of relapse or progression as post-auto-HSCT consolidation. Brentuximab vedotin is also approved for the treatment of relapsed primary cutaneous anaplastic large cell lymphoma or CD-30 expressing Mycosis Fungoides in patient who have received prior systemic therapy. It was also FDA approved in combination with chemotherapy for patients with previously untreated Stage III or IV CHL and for pediatric patients with previously untreated high risk CHL.

Hodgkin lymphoma (HL) is a B-cell lymphoma characterized by the presence of scarce, large neoplastic cells (mononucleated Hodgkin cells and multi-nucleated Reed-Sternberg cells) that reside in a complex mixture of non-neoplastic inflammatory cells. The morphology of the cells defines the two major subcategories of Hodgkin lymphoma: classical and nodular lymphocyte-predominant. In classical Hodgkin lymphoma, most of the Reed-Sternberg cells express CD30; however, in nodular lymphocyte-predominant Hodgkin lymphoma, Reed-Sternberg cells rarely express CD30. Systemic ALCL (sALCL) derives from mature T-cells and is considered one of the peripheral T-cell lymphomas. The cells of sALCL uniformly express CD30.

Current National Comprehensive Cancer Network (NCCN) guidelines support the use of brentuximab vedotin for the treatment of classical Hodgkin lymphoma, and in various types of B-cell and T-cell lymphomas.

POSITION STATEMENT:

Drug Waste Reduction: Additional medical necessity criteria for dose optimization may apply depending on the requested dose and member's benefit. Refer to Medical Coverage Guideline 09-J5000-54, Drug Waste Reduction.

Initiation of brentuximab vedotin (Adcetris®) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. The member's disease is CD30 positive*
2. The member's dosage of brentuximab does not exceed 1.8 mg/kg (or 180 mg if >100 kg) every 21 days†
3. The member has an indication listed in Table 1 and **ALL** indication-specific criteria are met:

Table 1: Indications for Use

Disease	Criteria for Use
Adult T-cell Leukemia/Lymphoma	When used for **ONE** of the following: 1. When used as a single agent for chronic high risk, acute, or lymphoma subtypes with an inadequate response to first-line therapy 2. When used in combination with cyclophosphamide, doxorubicin and prednisone for **ONE** of the following: a. Member has chronic high risk, acute, or lymphoma subtype b. Member has chronic low risk/smoldering subtype and an inadequate response to first-line therapy
Angioimmunoblastic T-cell lymphoma	When used for **ONE** of the following: 1. When used as a single agent as second-line or subsequent therapy, or palliative intent therapy for relapsed or refractory disease 2. When used in combination with cyclophosphamide, doxorubicin and prednisone (with or without etoposide) for previously untreated disease
Breast implant-associated Anaplastic Large Cell Lymphoma (ALCL)	When used for **ONE** of the following: 1. When used as a single agent as second-line or subsequent therapy for relapsed or refractory disease 2. When used as a single agent or in combination with cyclophosphamide, doxorubicin and prednisone as adjuvant therapy for **ONE** of the following: a. Localized disease to capsule/implant/breast and **ONE** of the following: i. Member had incomplete excision ii. Member had partial capsulectomy with residual disease b. Stage II, III or IV disease

Classical Hodgkin lymphoma (CHL)	When used for **ONE** of the following: 1. Relapsed or refractory CHL 2. **ONE** of the following: a. When used as a single agent for **ONE** of the following: i. The member has previously failed an autologous hematopoietic stem cell transplantation (auto-HSCT) for treatment of CHL ii. The member has previously failed one or more prior multi-agent chemotherapy regimens for CHL and brentuximab was not previously used iii. Member is over 60 years of age and brentuximab will be used as palliative therapy iv. Brentuximab will be used in a member at high risk of relapse or progression as consolidation or maintenance therapy following auto-HSCT b. When used as second-line or subsequent therapy in combination with one of the following if not previously used: i. bendamustine ii. nivolumab iii. ICE (ifosfamide, carboplatin, etoposide) 3. Stage III or IV CHL a. **ONE** of the following: i. Brentuximab will be used in combination with AVD (doxorubicin, vinblastine, and dacarbazine) ii. Brentuximab will be used as a component of BrECADD (brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone) iii. Brentuximab will be used in combination with dacarbazine iv. Brentuximab will used as a single agent before and after AVD v. Brentuximab will be used in combination with cyclophosphamide, doxorubicin, and prednisone (CHP)

	vi. Brentuximab will be used with nivolumab and the member is not a candidate for an anthracycline 4. Stage I or II CHL a. The member has unfavorable risk factors (e.g. bulky mediastinal or greater than 10 cm adenopathy, B symptoms) b. **ONE** of the following: i. Brentuximab will used as a single agent before and after AVD ii. Brentuximab will be used in combination with dacarbazine iii. Brentuximab will be used in combination with AVD (doxorubicin, vinblastine, and dacarbazine) iv. Brentuximab will be used in combination with cyclophosphamide, doxorubicin, and prednisone (CHP) v. Brentuximab will be used as a component of BrECADD (brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone) vi. Brentuximab will be used with nivolumab and the member is not a candidate for an anthracycline
Cutaneous Anaplastic Large Cell Lymphoma (ALCL)	When used for **ONE** of the following: 1. The member has multifocal lesions and brentuximab will be used as a single agent 2. The member has regional lymph node involvement and brentuximab will be used as a single agent or in combination with cyclophosphamide, doxorubicin and prednisone 3. The member's disease is refractory to prior systemic therapy and brentuximab will be used as a single agent or in combination with cyclophosphamide, doxorubicin and prednisone
Diffuse Large B-cell Lymphoma	When used for **ONE** of the following: 1. Used as a single agent and **ALL** of the following: a. Member has partial response, no response, progressive disease, or relapsed or refractory disease b. Member is not a candidate for transplant c. Used as second-line or subsequent therapy

	2. Used in combination with lenalidomide and rituximab and **ALL** of the following: a. Member has partial response, no response, progressive disease, or relapsed or refractory disease b. Used as third-line or subsequent therapy
Enteropathy associated T-cell lymphoma	When used for **ONE** of the following: 1. When used as a single agent as second-line or subsequent therapy, or palliative intent therapy for relapsed or refractory disease 2. When used in combination with cyclophosphamide, doxorubicin and prednisone (with or without etoposide) for previously untreated disease
Extranodal NK/T-cell Lymphoma (nasal type)	When used as a single agent and **ALL** of the following are met: 1. Member has relapsed or refractory disease 2. Member has an inadequate response or contraindication to asparaginase-based chemotherapy
Follicular T-cell lymphoma	When used for **ONE** of the following: 1. When used as a single agent as second-line or subsequent therapy, or palliative intent therapy for relapsed or refractory disease 2. When used in combination with cyclophosphamide, doxorubicin and prednisone (with or without etoposide) for previously untreated disease
Hepatosplenic T-cell Lymphoma	When used as a single agent after two or more previous lines of chemotherapy
High Grade B-cell Lymphomas (Not otherwise specified or Double/Triple Hit Lymphoma)	When used for **ONE** of the following: 1. Used as a single agent and **ALL** of the following: a. Member has partial response, no response, progressive disease, or relapsed or refractory disease b. Member is not a candidate for transplant c. Used as second-line or subsequent therapy 2. Used in combination with lenalidomide and rituximab and **ALL** of the following: a. Member has partial response, no response, progressive disease, or relapsed or refractory disease b. Used as third-line or subsequent therapy
HIV-related B-cell Lymphoma [includes HIV-related Diffuse Large B-cell Lymphoma (DLBCL), human herpes virus 8 (HHV8)-	When used for **ONE** of the following: 1. Used as a single agent and **ALL** of the following:

positive DLBCL, plasmablastic lymphoma, and primary effusion lymphoma]	a. Member has partial response, no response, progressive disease, or relapsed or refractory disease b. Member is not a candidate for transplant c. Used as second-line or subsequent therapy 2. Used as a single agent for relapsed plasmablastic lymphoma 3. Used in combination with lenalidomide and rituximab and **ALL** of the following: a. Member has partial response, no response, progressive disease, or relapsed or refractory disease b. Used as third-line or subsequent therapy
Lymphomatoid papulosis (LyP)	When used as a single agent and **ALL** of the following: 1. The member has extensive lesions 2. The member has relapsed or refractory disease 3. The member has tried and failed at least **TWO** prior treatments for LyP
Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL)	When used for **ONE** of the following: 1. When used as a single agent as second-line or subsequent therapy, or palliative intent therapy for relapsed or refractory disease 2. When used in combination with cyclophosphamide, doxorubicin and prednisone (with or without etoposide) for previously untreated disease
Mycosis fungoides (MF)/Sezary syndrome (SS)	**ONE** of the following: 1. When used as a single systemic agent (may be used with or without skin-directed therapy or local radiation therapy) for disease classified as **ONE** of the following: a. Stage IB-IIA disease with higher disease burden (e.g., predominately plaque disease, extensive skin involvement, blood involvement) b. Stage IIB disease with tumor lesions c. Stage III disease d. Stage IV disease e. Disease with large cell transformation f. Subsequent treatment for relapsed, persistent,or refractory to prior therapy
Nodal peripheral T-cell lymphoma with TFH phenotype	When used for **ONE** of the following: 1. When used as a single agent as second-line or subsequent therapy, or palliative intent therapy for relapsed or refractory disease

	2. When used in combination with cyclophosphamide, doxorubicin and prednisone (with or without etoposide) for previously untreated disease
Pediatric Hodgkin Lymphoma	When the member has **ONE** of the following: 1. Relapsed or refractory disease and **ONE** of the following: a. Brentuximab will be used as a single agent in a member at high risk of relapse as maintenance therapy following auto-HSCT b. Brentuximab will be used as re-induction or subsequent therapy (if not previously used) in combination with **ONE** of the following: i. bendamustine ii. nivolumab (with or without bendamustine) iii. gemcitabine 2. Stage III or IV disease in combination with ONE of the following: a. Cyclophosphamide, prednisone, dacarbazine (CAPDAC) b. Etoposide, prednisone, doxorubicin (AEPA) c. Doxorubicin, vincristine, etoposide, prednisone, cyclophosphamide (BV-AVE-PC) d. Doxorubicin, vinblastine, dacarbazine (Bv-AVD) e. Etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone (BrECADD) 3. Stage I or II disease with risk factors in combination with **ONE** of the following: a. Cyclophosphamide, prednisone, dacarbazine (CAPDAC) b. Etoposide, prednisone, doxorubicin(AEPA) c. Doxorubicin, vincristine, etoposide, prednisone, cyclophosphamide(BV-AVE-PC)
Pediatric Primary Mediastinal Large B-cell lymphoma	When used for **ONE** of the following: 1. If partial response achieved after therapy for relapsed or refractory disease in combination with **ONE** of the following: a. Nivolumab b. Pembrolizumab 2. When used in combination with nivolumab for the treatment of relapsed or refractory disease
Peripheral T-cell Lymphoma (not otherwise specified)	When used for **ONE** of the following:

	1. When used as a single agent as second-line or subsequent therapy, or palliative intent therapy for relapsed or refractory disease 2. When used in combination with cyclophosphamide, doxorubicin and prednisone (with or without etoposide) for previously untreated disease
Post-transplant Lymphoproliferative Disease (PTLD)	When used for **ONE** of the following: 1. Used as a single agent as second-line or subsequent therapy following chemotherapy for partial response, no response, progressive disease, or relapsed or refractory monomorphic PTLD (B-cell type) 2. Used in combination with cyclophosphamide, doxorubicin, and prednisone for monomorphic PTLD (T-cell type) 3. Used in combination with lenalidomide and rituximab and **ALL** of the following: a. Member has partial response, no response, progressive disease, or relapsed or refractory disease b. Used as third-line or subsequent therapy
Systemic Anaplastic Large Cell Lymphoma (ALCL)	When used for **ONE** of the following: 1. When used as a single agent as second-line or subsequent therapy, or palliative intent therapy for relapsed or refractory disease 2. When used in combination with cyclophosphamide, doxorubicin and prednisone (with or without etoposide) for previously untreated disease
Other FDA-approved or NCCN supported diagnosis (not previously listed above)	When **ONE** of the following is met: 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-aproved prescribing information (or package insert) 2. Indication AND usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation
Approval duration: 6 months (all indications) ***NOTE:** CD30-expressing (≥10%) is acceptable for Mycosis Fungoides, Sezary Syndrome, and cutaneous anaplastic large cell lymphoma. CD-30-positivity is not required for treatment of large B-cell lymphoma (LBCL), Diffuse LBCL (DLBCL), DLBCL not otherwise specified (NOS), high-grade B-cell lymphomas, HIV-related B-cell lymphomas, or post-transplant lyphoproliferative disorders. Quest Diagnostics® can perform the CD30 immunohistochemical assay.	

Continuation of brentuximab vedotin (Adcetris®) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization for brentuximab has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of an indication listed in Table 1 **OR** the member previously met all indication-specific initiation criteria.
2. The member does **NOT** have progressive disease during treatment with brentuximab per treating physician attestation.
3. Dosage does not exceed 1.8 mg/kg (or 180 mg if >100 kg) every 21 days†

Approval duration: 1 year

† For previously untreated stage III or IV CHL, an alternative dose of 1.2 mg/kg (or 120 mg if >100 kg) every 14 days may be used.

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: Brentuximab is indicated for treatment of the following:

- Adult patients with previously untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine
    - 1.2 mg/kg (max 120 mg) administered over 30 minutes every 2 weeks for a maximum of 12 doses, disease progression, or unacceptable toxicity
- Pediatric patients 2 years and older with previously untreated high risk classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vincristine, etoposide, prednisone, and cyclophosphamide
    - 1.8 mg/kg (max 180 mg) administered intravenously (IV) over 30 minutes every 3 weeks for a maximum of 5 doses
- Adult patients with classical Hodgkin lymphoma (HL) at high risk of relapse or progression as post autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation
    - 1.8 mg/kg (max 180 mg) administered intravenously (IV) over 30 minutes every 3 weeks. Initiate treatment within 4 to 6 weeks post-auto-HSCT or upon recovery from auto-HSCT. Treatment should continue for CHL consolidation until a maximum of 16 cycles, disease progression, or unacceptable toxicity
- Adult patients after failure of auto-HSCT or after failure of at least 2 prior multi-agent chemotherapy regimens in persons who are not auto-HSCT candidates
    - 1.8 mg/kg (max 180 mg) administered intravenously (IV) over 30 minutes every 3 weeks. Treatment is continued until disease progression or unacceptable toxicity
- Adult patients with previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified, in combination with cyclophosphamide, doxorubicin, and prednisone
    - 1.8 mg/kg up to a maximum of 180 mg every 3 weeks for 6 to 8 doses. Treatment is continued until disease progression or unacceptable toxicity
- Adult patients with systemic anaplastic large cell lymphoma (sALCL) after failure of at least one prior multi-agent chemotherapy regimen

- 1.8 mg/kg (max 180 mg) administered intravenously (IV) over 30 minutes every 3 weeks. Treatment is continued until disease progression or unacceptable toxicity.

- Adult patients with primary cutaneous anaplastic large cell lymphoma or CD30-expressing mycosis fungoides (MF) who have received prior systemic therapy
  - 1.8 mg/kg (max 180 mg) administered intravenously (IV) over 30 minutes every 3 weeks. Treatment should continue until a maximum of 16 cycles, disease progression, or unacceptable toxicity
- Relapsed or refractory large B-cell lymphoma including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), DLBCL arising from indolent lymphoma, or high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy who are not candidates for auto-HSCT or chimeric antigen receptor (CAR) T-cell therapy in combination with lenalidomide and rituximab
  - 1.2 mg/kg (max 120 mg) in combination with lenalidomide and rituximab administered over 30 minutes every 3 weeks until disease progression, or unacceptable toxicity

Dose Adjustments

- Peripheral Neuropathy: manage using a combination of dose delay and reduction. See prescribing information for dose recommendations. For Grade 4 peripheral neuropathy, brentuximab should be discontinued.
- Neutropenia: manage using a combination of dose delay and reduction. See prescribing information for dose recommendations
- Renal impairment: No adjustment is needed in patients with mild to moderate impairment (CrCl ≥30 mL/min). Use should be avoided in patients with severe impairment (CrCl <30 mL/min).
- Hepatic impairment: For mild impairment (Child-Pugh A) the dosage should be reduced. See prescribing information for dose recommendations. Use should be avoided in patients with moderate (Child-Pugh B) or severe (Child-Pugh C) impairment.

Drug Availability: brentuximab is available as a 50 mg single-use vial for reconstitution.

PRECAUTIONS:

Boxed Warning:

JC virus infection resulting in progressive multifocal leukoencephalopathy (PML) and death can occur in persons receiving brentuximab.

CONTRAINDICATIONS:

Concomitant use with bleomycin is contraindicated due to pulmonary toxicity.

WARNINGS/PRECAUTIONS

- Peripheral neuropathy: Treating physicians should monitor members for neuropathy and institute dose modifications accordingly.
- Anaphylaxis and infusion reactions: If an infusion reaction occurs, the infusion should be interrupted and appropriate medical management instituted. If anaphylaxis occurs, the infusion should be discontinued immediately and appropriate medical management instituted.
- Hematologic Toxicities: Prolonged (≥1 week) severe neutropenia and Grade 3 or Grade 4 thrombocytopenia or anemia can occur. Monitor complete blood counts prior to each dose of brentuximab and monitor for fever. If Grade 3 or 4 neutropenia develops, manage by dose

delays, reductions or discontinuation. Administer G-CSF starting with cycle 1 for previously untreated Stage III or IV CHL when brentuximab is used in combination with chemotherapy.

- Serious infections and opportunistic infections: Closely monitor patients for the emergence of bacterial, fungal or viral infections.
- Tumor Lysis Syndrome: persons with rapidly proliferating tumor and high tumor burden are at risk of tumor lysis syndrome and these individuals should be monitored closely and appropriate measures taken.
- Hepatotoxicity: Serious cases of hepatotoxicity, including fatal outcomes, have occurred. Monitor liver enzymes and bilirubin. Patients experiencing new, worsening, or recurrent hepatotoxicity may require a delay, change in dose, or discontinuation.
- Pulmonary Toxicity: Evaluate new or worsening pulmonary symptoms.
- Progressive Multifocal Leukoencephalopathy (PML): Monitor neurologic function; hold brentuximab if PML is suspected and discontinue brentuximab if PML is confirmed.
- Serious Dermatologic Reactions: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), including fatal outcomes, have been reported. If SJS or TEN occurs, discontinue brentuximab and administer appropriate medical therapy.
- Gastrointestinal complications: Monitor patients for new or worsening symptoms.
- Hyperglycemia: Monitor patients with new hyperglycemia and manage with anti-hyperglycemic medication as indicated.
- Use in pregnancy: Fetal harm can occur. Pregnant women should be advised of the potential hazard to the fetus.

BILLING/CODING INFORMATION:

HCPCS Coding

J9042	Injection, brentuximab vedotin, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

B20	Human immunodeficiency virus (AIDs related disease)
C81.10 – C81.79	Hodgkin lymphoma
C81.90 – C81.99	Hodgkin lymphoma, unspecified
C82.00 – C82.99	Follicular lymphoma
C83.30 – C83.398	Diffuse large B-cell lymphoma
C83.80 – C83.89	Other non-follicular lymphoma
C83.90 – C83.99	Non-follicular (diffuse) lymphoma, unspecified
C84.00 – C84.09	Mycosis fungoides
C84.10 – C84.19	Sézary disease
C84.40 – C84.49	Peripheral T-cell lymphoma, not classified
C84.60 – C84.79, C84.7A	Anaplastic large cell lymphoma
C84.90 – C84.99	Mature T/NK-cell lymphomas unspecified
C84.Z0 – C84.Z9	Other mature T/NK-cell lymphomas
C85.10 – C85.19	Unspecified B-cell lymphoma
C85.20 – C85.29	Mediastinal (thymic) large B-cell lymphoma
C85.80 – C85.89	Other specified types of non-Hodgkin lymphoma
C86.00 – C86.60	Other specified types of T/NK-cell lymphomas
C91.50 – C91.52	Adult T-cell lymphoma/leukemia
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)

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) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

B Symptoms: The presence of one or more of the following systemic symptoms within 6 months prior to diagnosis are an unfavorable risk factor: (1) unexplained fevers >38 degrees C, (2) drenching night sweats, or (3) weight loss >10% of body weight.

Hodgkin lymphoma (HL): an uncommon malignancy involving lymph nodes and the lymphatic system. The World Health Organization (WHO) classification divides HL into two main types: classical Hodgkin lymphoma (CHL) and nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL). In the U.S., CHL account for 95% of all HL cases. Classical HL is divided into four subtypes: nodular sclerosis CHL, mixed cellularity, lymphocyte-depleted CHL, and lymphocyte-rich CHL.

Primary treatment of CHL: Clinical management involves initial treatment with chemotherapy or combined modality therapy (i.e., chemotherapy + radiation), followed by restaging at the completion of chemotherapy to assess treatment response. The specific therapy and follow-up recommendations are based on the staging of the CHL; however, all recommendations have an initial multi-agent chemotherapy component.

Progressive multifocal leukoencephalopathy (PML): also known as progressive multifocal leukoencephalitis, is a rare and usually fatal viral disease that is characterized by progressive damage or inflammation of the white matter of the brain at multiple locations. It occurs almost exclusively in people with severe immune deficiency, such as transplant patients on immunosuppressive medications, patients receiving certain kinds of chemotherapy, AIDS patients and patients treated with other agents that suppress the immune system. It is caused by a virus, the JC virus, which is normally present and kept under control by the immune system. Immunosuppressive drugs prevent the immune system from controlling the virus.

Staging of HL: After initial diagnosis, patients are divided into either stage I-II (early stage) or stage III-IV (advanced-stage) disease based on the Ann Arbor staging system. Patients with stage I-II are further classified based on presence or absence of unfavorable risk factors into stage IA-IIA (favorable), stage I-II (unfavorable with bulky disease), and stage I-II (unfavorable with non-bulky disease). The unfavorable risk factors for stage I-II disease include bulky mediastinal disease or bulky disease greater than 10 cm, B symptoms, erythrocyte sedimentation rate (ESR) >50, and >3 nodal site of disease. For stage III-IV disease, an International Prognostic Score (IPS) is determined based on the number of adverse prognostic factors present at diagnosis. These 7 factors include: age >45 years, male gender, stage IV disease, albumin <4 g/dL, hemoglobin <10.5 g/dL, WBC <15,000/m^3, and lymphocyte count <600/mm^3 or <8% of WBC.

Stevens–Johnson syndrome (SJS): a form of a life-threatening skin condition, in which cell death causes the epidermis to separate from the dermis. The syndrome is thought to be a hypersensitivity complex that affects the skin and the mucous membranes. Although the majority of cases are idiopathic

(without a known cause), the main class of known causes is medication, followed by infections and, rarely, cancers.

Tumor Lysis syndrome (TLS): a group of metabolic complications that can occur after treatment of cancer, usually lymphomas and leukemias, and sometimes even without treatment. These complications are caused by the break-down products of dying cancer cells and include hyperkalemia, hyperphosphatemia, hyperuricemia and hyperuricosuria, hypocalcemia, and consequent acute uric acid nephropathy and acute renal failure.

RELATED GUIDELINES:

Autologous Bone Marrow and Stem Cell Transplantation, 02-38241-01

Bortezomib (Velcade®) IV, 09-J0000-92

Carboplatin (Paraplatin®) IV, 09-J0000-93

Doxorubicin HCl Liposome (Doxil®) IV, 09-J0000-91

Gemcitabine (Gemzar®), 09-J0000-96

Granulocyte Colony Stimulating Factors, 09-J0000-62

Intensity-Modulated Radiation Therapy (IMRT), 04-77260-22

Lenalidomide (Revlimid®), 09-J0000-80

Oxaliplatin (Eloxatin®) IV, 09-J1000-00

Pralatrexate (Folotyn®) IV, 09-J1000-18

Rituximab (Rituxan®), 09-J0000-59

Vinorelbine Tartrate (Navelbine®) IV, 09-J1000-03

OTHER:

None.

REFERENCES:

1. Adcetris (brentuximab vedotin) [package insert]. Seattle Genetics, Inc. Bothell (WA): Feb 2025.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2025. Accessed 07/30/25
3. Conners JM, Jurczak W, Straus DJ et al. Brentuximab vedotin with chemotherapy for Stage III or IV Hodgkin's Lymphoma. N Engl J Med. 2018 Jan; 378 (4): 331-344.
4. Fanale MA, Horwitz SM, Forero-Torres A, et al. Brentuximab vedotin in the front-line treatment of patients with CD30+ peripheral T-cell lymphomas: results of a phase I study. J Clin Oncol. 2014 Oct 1;32(28):3137-43. doi: 10.1200/JCO.2013.54.2456. Epub 2014 Aug 18.
5. Horwitz SM, Advani RH, Bartlett NL, et al. Objective responses in relapsed T-cell lymphomas with single-agent brentuximab vedotin. Blood. 2014 May 15;123(20):3095-100. doi: 10.1182/blood-2013-12-542142. Epub 2014 Mar 20.
6. Jacobsen ED, Sharman JP, Oki Y, et al. Brentuximab vedotin demonstrates objective responses in a phase 2 study of relapsed/refractory DLBCL with variable CD30 expression. Blood. 2015 Feb 26;125(9):1394-402. doi: 10.1182/blood-2014-09-598763. Epub 2015 Jan 8.
7. Mehra T, Ikenberg K, Moos RM, et al. Brentuximab as a treatment for CD30+ mycosis fungoides and Sézary syndrome. JAMA Dermatol. 2015 Jan;151(1):73-7. doi: 10.1001/jamadermatol.2014.1629.

8. Micromedex® Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 07/30/25.
9. Moskowitz CH, Nademanee A, Masszi T, et al. Brentuximab vedotin as consolidation therapy after autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2015 May 9;385(9980):1853-62.
10. National Comprehensive Cancer Network. Cancer Guidelines. Cancer Guidelines and Drugs and Biologics Compendium. Accessed 06/12/26.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 08/13/25.

GUIDELINE UPDATE INFORMATION:

11/15/11	New Medical Coverage Guideline.
08/15/12	Review and revision to guideline; consisting of updating precautions, coding and references.
01/01/13	Annual HCPCS Update: added HCPCS code J9042.
08/15/13	Review and revision to guideline; consisting of revising position statement to require CD30 positivity and brentuximab use as monotherapy; revised description section; revised and reformatted dosage/administration and precautions section; updated coding, program exceptions and references.
04/15/14	Revision to guideline; consisting of removing 16-cycle limit.
08/15/14	Review and revision to guideline; consisting of updating references.
08/15/15	Review and revision to guideline; consisting of description, position statement, dosage/administration, precautions, billing/coding information, and references.
10/15/15	Revision to guideline consisting of updating description and dosage/administration sections, references, and definitions, and reformatting the position statement.
11/01/15	Revision: ICD-9 Codes deleted.
08/15/16	Review and revision to guideline; consisting of updating position statement, coding and references.
10/01/16	Update to ICD-10 codes.
08/15/17	Review and revision to guideline; consisting of updating position statement, coding, and references.
03/15/18	Revision to guideline; consisting of updating position statement, coding, and references.
05/15/18	Revision to guideline; consisting of updating position statement and references.
07/15/18	Review and revision to guideline; consisting of updating position statement, coding and references.
01/15/19	Revision to guideline; consisting of updating position statement and references.
02/15/19	Revision to guideline; consisting of updating position statement and references.
08/15/19	Review and revision to guideline; consisting of updating position statement, coding and references.
08/15/20	Review and revision to guideline; consisting of updating position statement and references.
08/15/21	Review and revision to guideline; consisting of updating position statement, coding, and references
10/01/21	ICD-10 coding update.
08/15/22	Review and revision to guideline; consisting of updating the position statement and references.
10/15/23	Review and revision to guideline; consisting of updating the position statement for CHL, pediatric primary mediastinal large B-cell lymphoma, Mycosis fungoides (MF)/Sezary

	syndrome (SS), post-transplant lymphoproliferative disorder, and HIV-related B-cell lymphomas.
10/01/24	ICD-10 coding update.
10/15/24	Review and revision to guideline; consisting of updating the position statement for Adult T-cell Leukemia/Lymphoma, CHL, and Mycosis Fungoides/Sezary syndrome.
09/15/25	Review and revision to guideline; consisting of updating the position statement for Diffuse large B-cell lymphoma, High grade B-cell lymphoma, HIV-related B-cell lymphomas, PTLD, Mycosis Fungoides/Sezary syndrome, Classic Hodgkin Lymphoma, pediatric Hodgkin Lymphoma, and pediatric primary mediastinal lymphoma per NCCN.
06/01/26	Revision: Added Drug Waste Reduction statement to the Position Statement.
07/15/26	Revision to guideline consisting of updating the position statement and NCCN indications.