Clinical Policy: Brentuximab Vedotin (Adcetris)

Reference Number: CP.PHAR.303
Effective Date: 02.01.17
Last Review Date: 08.23
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Brentuximab vedotin for injection (Adcetris®) is a CD30-directed antibody-drug conjugate.

FDA Approved Indication(s)

Adcetris is indicated for the treatment of adult patients with:

- Classical Hodgkin lymphoma:
  - Previously untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine
  - cHL at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation
  - cHL after failure of auto-HSCT or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates
- T-cell lymphomas:
  - 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
  - sALCL after failure of at least one prior multiagent chemotherapy regimen
- Primary cutaneous lymphomas:
  - Primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) who have received prior systemic therapy

Adcetris is indicated for the treatment of pediatric patients 2 years old and older with:

- Classical Hodgkin lymphoma:
  - Previously untreated high risk cHL, in combination with doxorubicin, vincristine, etoposide, prednisone, and cyclophosphamide

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Adcetris is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Classical Hodgkin Lymphoma in Adults (must meet all)**:**

1. Diagnosis of cHL;

2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years*;
   ** If age is between 2 to 21 years, consider using I.B cHL in Pediatric and Adolescent Patients below.*
4. If previously untreated disease, prescribed in one of the following ways (a or b):
   a. In combination with AVD (doxorubicin, vinblastine, and dacarbazine);
   b. For age > 60 years: In combination with dacarbazine;
5. If released or refractory disease, prescribed in one of the following ways (a-e):
   a. As a single agent;
   b. In combination with bendamustine;
   c. In combination with ICE (ifosfamide, carboplatin, etoposide);
   d. In combination with nivolumab;
   e. Following high-dose therapy and autologous stem cell rescue;
6. Request meets one of the following (a or b):**
   a. Dose does not exceed (i, ii, or iii):
      i. Previously untreated Stage III or IV cHL: 1.2 mg/kg up to 120 mg every 2 weeks for a maximum of 12 doses;
      ii. cHL consolidation: 1.8 mg/kg up to 180 mg every 3 weeks for a maximum of 16 cycles;
      iii. Relapsed cHL: 1.8 mg/kg up to 180 mg every 3 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   ***Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

B. Classical Hodgkin Lymphoma in Pediatric and Adolescent Patients (must meet all)**:**
1. Diagnosis of cHL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age between 2 years to 21 years;
4. One of the following (a, b, or c):
   a. If previously untreated: Prescribed as a component of Bv-AVE-PC (brentuximab vedotin, doxorubicin, vincristine, etoposide, prednisone, cyclophosphamide) or AEPA (brentuximab vedotin, etoposide, prednisone, doxorubicin);
   b. If following AEPA: Prescribed as a component of CAPDAC (cyclophosphamide, brentuximab vedotin, prednisone, dacarbazine);
   c. For relapsed or refracory disease (i or ii):
      i. Prescribed in combination with involved-site radiation therapy (ISRT) or bendamustine/nivolumab/gemcitabine;
      ii. Prescribed following high-dose therapy and autologous stem cell rescue;
5. For all requests except when prescribed in combination with ISRT or bendamustine/nivolumab/gemcitabine: Disease is classified as high risk (*see Appendix D*);
6. Request meets one of the following (a or b):*
   a. Dose does not exceed: 1.8 mg/kg up to 180 mg every 3 weeks for a maximum of 5 doses;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

C. T-Cell Lymphomas (must meet all)**:**
1. Diagnosis of one of the following (a, b, c, d, or e):
   a. PTCL - any of the following subtypes/histologies (i or ii):
      i. sALCL;
      ii. PTCL, including but not limited to the following (1, 2, 3, 4, or 5):
         1) Angioimmunoblastic T-cell lymphoma;
         2) Enteropathy-associated T-cell lymphoma;
         3) Monomorphic epitheliotropic intestinal T-cell lymphoma;
         4) Nodal PTCL with TFH phenotype;
         5) Follicular T-cell lymphoma;
   b. Breast implant-associated ALCL (off-label);
   c. Adult T-cell leukemia/lymphoma (off-label);
   d. Relapsed or refractory extranodal NK/T-cell lymphoma (off-label);
   e. Hepatosplenic T-cell lymphoma after failure of two first-line therapy regimens (off-label);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For all requests except ALCL: Disease is CD30-positive;
5. Prescribed as a single agent or in combination with CHP (cyclophosphamide, doxorubicin, prednisone);
6. Request meets one of the following (a, b, or c):*
   a. Previously untreated sALCL or other CD30-positive PTCL including angioimmunoblastic T-cell lymphoma: Dose does not exceed 1.8 mg/kg up to 180 mg every 3 weeks with each cycle of chemotherapy for 6 to 8 doses;
   b. Relapsed sALCL: Dose does not exceed 1.8 mg/kg up to 180 mg every 3 weeks;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

D. Primary Cutaneous CD30+ T-Cell Lymphoproliferative Disorders (must meet all)**:**
1. Diagnosis of one of the following (a, b, or c):
   a. pcALCL;
   b. Cutaneous ALCL with multifocal lesions or lymph node positive (off-label);
   c. Lymphomatoid papulosis - as subsequent therapy for relapsed/refractory disease (off-label);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Disease is CD30-positive;
5. Request meets one of the following (a or b):*
   a. Relapsed pcALCL: Dose does not exceed 1.8 mg/kg up to 180 mg every 3 weeks for a maximum of 16 cycles;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

E. Mycosis Fungoides/Sezary Syndrome (must meet all)**:**
1. Diagnosis of MF or Sezary syndrome (off-label);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):*
   a. Relapsed CD30-positive MF: Dose does not exceed 1.8 mg/kg up to 180 mg every 3 weeks for a maximum of 16 cycles;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

F. B-Cell Lymphomas (off-label) (must meet all)**:**
1. Diagnosis of one of the following (a, b, c, or d):
   a. Diffuse large B-cell lymphoma;
   b. High-grade B-cell lymphoma;
   c. HIV-related B-cell lymphoma;
   d. Monomorphic post-transplant lymphoproliferative disorder (PTLD) (B- or T-cell type);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. One of the following (a or b):
   a. Age ≥ 18 years;
   b. Age < 18 years and both of the following (i and ii):
      i. Relapsed or refractory primary mediastinal large B-cell lymphoma;
      ii. Prescribed in combination with nivolumab or pembrolizumab;
4. Disease is CD30-positive;
5. For subtypes other than monomorphic PTLD (T-cell type), both of the following (a and b):
   a. Adcetris is prescribed as subsequent therapy;
   b. Member is not a candidate for allogeneic or autologous stem cell transplant;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

G. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Adcetris for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed (i, ii, iii, iv, v, vi, vii, or viii):
      i. Previously untreated Stage III or IV cHL in adults: 1.2 mg/kg up to 120 mg every 2 weeks for a maximum of 12 doses;
      ii. Previously untreated high risk cHL in pediatric and adolescent patients: 1.8 mg/kg up to 180 mg every 3 weeks for a maximum of 5 doses;
      iii. cHL consolidation in adults: 1.8 mg/kg up to 180 mg every 3 weeks for a maximum of 16 cycles;
      iv. Relapsed cHL in adults: 1.8 mg/kg up to 180 mg every 3 weeks;
      v. Previously untreated sALCL or other CD30-positive PTCL including angioimmunoblastic T-cell lymphoma in adults: 1.8 mg/kg up to 180 mg every 3 weeks with each cycle of chemotherapy for 6 to 8 doses;
      vi. Relapsed sALCL in adults: 1.8 mg/kg up to 180 mg every 3 weeks;
      vii. Relapsed pcALCL in adults: 1.8 mg/kg up to 180 mg every 3 weeks for a maximum of 16 cycles;
      viii. Relapsed CD30-positive MF in adults: 1.8 mg/kg up to 180 mg every 3 weeks for a maximum of 16 cycles;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

cHL: classical Hodgkin lymphoma
FDA: Food and Drug Administration
HSCT: hematopoietic stem cell transplantation
ISRT: involved-site radiation therapy
MF: mycosis fungoides
NCCN: National Comprehensive Cancer Network
pcALCL: primary cutaneous anaplastic large cell lymphoma
PTCL: peripheral T-cell lymphoma
sALCL: systemic analplastic large cell lymphoma
SS: Sezary syndrome

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): concomitant use with bleomycin due to pulmonary toxicity
- Boxed warning(s): progressive multifocal leukoencephalopathy

Appendix D: Definitions of High Risk Disease

Per NCCN, high risk disease is defined as:

- Stage IIB with bulk disease*
  **Large mediastinal adenopathy (LMA): a mediastinal mass where the tumor diameter is > 1/3 the maximal thoracic diameter on an upright posteroanterior (PA) chest radiograph OR large extra-mediastinal nodal aggregate: a contiguous extramediastinal nodal aggregate that measures > 6 cm in the longest transverse diameter (transaxial measurement) or craniocaudal dimension (measured on reformatted computed tomography)*
- Stage IIIA
- Stage IIIB with E-lesions**
  ***Localized involvement of extralymphatic tissue (by contiguous growth from an involved lymph node or in close anatomic relation) that is treatable by irradiation*
- Stage IV

Per the Adcetris pediatric cHL pivotal study, high risk was defined as the following Ann Arbor stages:

- Stage IIB with bulk disease (*see definition of bulk disease above*)
- Stage IIIB
- Stage IVA
- Stage IVB

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Previously untreated Stage III or IV cHL in adults	1.2 mg/kg IV up to a maximum of 120 mg in combination with chemotherapy. Administer every 2 weeks until a maximum of 12 doses, disease progression, or unacceptable toxicity.	120 mg every 2 weeks up to 12 doses
Previously untreated high risk cHL in pediatric and adolescent patients	1.8 mg/kg IV up to a maximum of 180 mg in combination with chemotherapy. Administer every 3 weeks with each cycle of chemotherapy for a maximum of 5 doses, disease progression, or unacceptable toxicity.	180 mg every 3 weeks up to 5 doses
cHL consolidation in adults	1.8 mg/kg IV up to a maximum of 180 mg. Initiate Adcetris treatment within 4-6 weeks post-autoHSCT or upon recovery from auto-HSCT. Administer every 3 weeks until a maximum of 16 cycles, disease progression, or unacceptable toxicity.	180 mg every 3 weeks up to 16 cycles
Relapsed cHL in adults	1.8 mg/kg IV up to a maximum of 180 mg. Administer every 3 weeks until disease progression or unacceptable toxicity.	180 mg every 3 weeks
Previously untreated sALCL or other CD30-expressing PTCLs in adults	1.8 mg/kg IV up to a maximum of 180 mg in combination with cyclophosphamide, doxorubicin, and prednisone. Administer every 3 weeks with each cycle of chemotherapy for 6 to 8 doses.	180 mg every 3 weeks up to 6 to 8 doses
Relapsed sALCL in adults	1.8 mg/kg IV up to a maximum of 180 mg. Administer every 3 weeks until disease progression or unacceptable toxicity.	180 mg every 3 weeks
Relapsed pcALCL or CD30-expressing MF in adults	1.8 mg/kg IV up to a maximum of 180 mg. Administer every 3 weeks until a maximum of 16 cycles, disease progression, or unacceptable toxicity.	180 mg every 3 weeks up to 16 cycles

VI. Product Availability

Single-use vial: 50 mg for reconstitution

VII. References

1. Adcetris Prescribing Information. Bothell, WA: Seagen, Inc.; November 2022. Available at: http://adcetrisupdate.com/. Accessed May 17, 2023.

2. Castellino SM, et al. Brentuximab vedotin with chemotherapy in pediatric high-risk Hodgkin's lymphoma. New Engl J Med 2022; 387(18):1649-1660.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed May 17, 2023.
4. National Comprehensive Cancer Network. Hodgkin Lymphoma Version 2.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf. Accessed May 17, 2023.
5. National Comprehensive Cancer Network.Pediatric Hodgkin Lymphoma Version 2.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_hodgkin.pdf. Accessed May 17, 2023.
6. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version 1.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed May 17, 2023.
7. National Comprehensive Cancer Network. T-Cell Lymphomas Version 1.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed May 17, 2023.
8. National Comprehensive Cancer Network. B-Cell Lymphomas Version 3.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed May 17, 2023.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9042	Injection, brentuximab vedotin, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Q3 2019 annual review; NCCN and FDA-approved uses summarized for clarity; NCCN recommended uses added - B-cell lymphomas, additional T-cell lymphomas; references reviewed and updated.	05.14.19	08.19
Added Commercial line of business to policy.	10.08.19	
Q3 2020 annual review: HIM line of business added; per NCCN, breast-implant associated ALCL stage restriction removed, primary mediastinal large B-cell lymphoma added, post-transplant lymphoproliferative disorder limited to monomorphic PTLD (T-cell type) inclusive of primary therapy; references reviewed and updated.	05.12.20	08.20
3Q 2021 annual review: no significant changes; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	03.16.21	08.21
Added legacy WCG line of business (WCG.CP.PHAR.303 to be retired); for legacy WCG, initial approval duration shortened from 12 months to 6 months.	12.07.21	02.22
3Q 2022 annual review: per NCCN Compendium clarified extranodal NK/T-cell lymphoma should be in the relapsed or refractory setting	05.02.22	08.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
and removed requirement for nasal type; clarified hepatosplenic T-cell lymphoma should be after two first-line therapy regimens; references reviewed and updated.		
RT4: New indication of previously untreated high risk cHL in pediatric and adolescent patients added to policy. Template changes applied to other diagnoses/indications and continued therapy section.	12.16.22	
3Q 2023 annual review: for adult cHL, added specific regimens for use per both FDA and NCCN; for pediatric cHL, moved specific staging requirements for high risk disease to Appendix D to also allow for NCCN high risk definition and updated criteria per NCCN, including requirements for use in combination with chemotherapy as well as allowance for use as subsequent therapy; for T-cell lymphomas, clarified that CD30-positive disease requirement does not apply to ALCL and added requirement for use as a single agent or in combination with CHP per NCCN; for cutaneous ALCL, added pathway for disease multifocal lesions per NCCN; for MF/SS, removed requirement for CD30-positive disease per NCCN; for B-cell lymphomas, removed specific subtypes of DLBCL to simplify criteria, revised "AIDS-related" to "HIV-related", added B-cell type monomorphic PTLD, added pathway for pediatric primary mediastinal large B-cell lymphoma, and added that member is not a transplant candidate for all requests except T-cell type monomorphic PTLD per NCCN; references reviewed and updated.	05.17.23	08.23

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy,

contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.