Clinical Policy: Brentuximab Vedotin (Adcetris)

Reference Number: CP.PHAR.303
Effective Date: 02.01.17
Last Review Date: 08.19
Line of Business: Commercial, Medicaid, HIM-Medical Benefit

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
  - Classical Hodgkin lymphoma at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation
  - Classical Hodgkin lymphoma 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

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 (must meet all)**:**

1. Diagnosis of cHL;
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. Dose does not exceed (i or ii):

i. Previously untreated Stage III or IV cHL: dose does not exceed 1.2 mg/kg up to 120 mg every 2 weeks for a maximum of 12 doses;
ii. cHL consolidation: dose does not exceed 1.8 mg/kg up to 180 mg every 3 weeks for a maximum of 16 cycles;
iii. Relapsed cHL: dose does not exceed 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*).

Approval duration: 6 months

B. T-Cell Lymphomas (must meet all)**:**

1. One of the following diagnoses (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 (a, b, c, d, or e):
         a) Angioimmunoblastic T-cell lymphoma;
         b) Enteropathy-associated T-cell lymphoma;
         c) Monomorphic epitheliotropic intestinal T-cell lymphoma;
         d) Nodal peripheral T-cell lymphoma with TFH phenotype;
         e) Follicular T-cell lymphoma;
   b. Breast implant-associated ALCL (Stage II to IV) (off-label);
   c. Adult T-cell leukemia/lymphoma (off-label);
   d. Extranodal NK/T-cell lymphoma, nasal type (off-label);
   e. Hepatosplenic Gamma-Delta T-cell lymphoma (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, 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*).

Approval duration: 6 months

C. 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 and lymph node positive (off-label);
   c. Lymphomatoid papulosis - as subsequent therapy for relapsed/refractory disease (off-label);
2. Disease is CD30-positive;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 18 years;
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)*.

Approval duration: 6 months

D. 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. Disease is CD30-positive;
5. 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)*.

Approval duration: 6 months

E. B-Cell Lymphomas (off-label) (must meet all)**:**
1. Diagnosis of one of the following (a or b):
   a. Diffuse large B-cell lymphoma, including but not limited to (i or ii):
      i. Follicular lymphoma that has undergone histologic transformation to diffuse large B-cell lymphoma;
      ii. Marginal zone lymphoma that has undergone histologic transformation to diffuse large B-cell lymphoma;
   b. High-grade B-cell lymphoma;
   c. AIDS-related B-cell lymphoma;
   d. Post-transplant lymphoproliferative disorder;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Disease is CD30-positive;
5. Adcetris is prescribed as subsequent therapy;
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*).

Approval duration: 6 months

F. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, CP.PMN.53 for Medicaid and HIM-Medical Benefit.

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, or vii):
      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;
      iv. Previously untreated sALCL or other CD30-positive PTCL including angioimmunoblastic T-cell lymphoma: 1.8 mg/kg up to 180 mg every 3 weeks with each cycle of chemotherapy for 6 to 8 doses;
      v. Relapsed sALCL: 1.8 mg/kg up to 180 mg every 3 weeks;
      vi. Relapsed pcALCL: 1.8 mg/kg up to 180 mg every 3 weeks for a maximum of 16 cycles;
      vii. Relapsed CD30-positive MF: 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*).

Approval duration: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, CP.PMN.53 for Medicaid and HIM-Medical Benefit.

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, CP.PMN.53 for Medicaid and HIM-Medical Benefit 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
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

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Previously untreated Stage III or IV cHL	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
cHL consolidation	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	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	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	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	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: Seattle Genetics, Inc.; November 2018. Available at: http://adcetrisupdate.com/. Accessed May 17, 2019.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed May 17, 2019.

3. National Comprehensive Cancer Network. Hodgkin Lymphoma Version 1.2019. Available at www.nccn.org. Accessed May 17, 2019.
4. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version 2.2019. Available at www.nccn.org. Accessed May 17, 2019.
5. National Comprehensive Cancer Network. T-Cell Lymphomas Version 2.2019. Available at www.nccn.org. Accessed May 17, 2019.
6. National Comprehensive Cancer Network. B-Cell Lymphomas Version 3.2019. Available at www.nccn.org. Accessed May 17, 2019.
7. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed May 17, 2019.

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
Policy split from CP.PHAR.182 Excellus Oncology.	01.01.17	02.17
Age and dosing added Safety information removed. NCCN recommended uses added separately.	09.05.17	11.17
3Q18 annual review: Added HIM Medical; added new FDA approved status for pcALCL and MF indications (previously off-label coverage) and previously untreated cHL in combination with chemotherapy; added examples of prerequisite drugs for HL, sALCL, adult T-cell leukemia/ lymphoma, and LyP; references reviewed and updated.	04.30.18	08.18
No significant changes, updated Non-Hodgkin T-Cell Lymphomas criteria set to allow use as first-line therapy for PTCL to align with updated FDA-approved indication.	12.05.18	
PI directed dosing details (i.e., weight-based dosing, and maximum dose and duration) are added to all criteria sets in Sections I.A. and II, and the dosing table in Section V; parentheticals are added to each criteria set indicating off-label NCCN recommended uses which would require supportive dosing literature. Reference to CD30+ disease is expanded to all indications under the Primary Cutaneous CD30+ T-cell Lymphoproliferative Disorders criteria set for clarity.	05.03.19	
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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added Commercial line of business to policy.	10.08.19	

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.

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.