Clinical Policy: Brentuximab Vedotin (Adcetris)

Reference Number: CP.PHAR.303
Effective Date: 02.01.17
Last Review Date: 08.18
Line of Business: 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:

- Previously untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with chemotherapy
- 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
- Systemic anaplastic large cell lymphoma (sALCL) after failure of at least one prior multiagent chemotherapy regimen
- 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. Hodgkin Lymphoma (must meet all)**:**

1. Diagnosis of classical Hodgkin lymphoma (HL);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Meets (a, b, c, d, or e):
   a. After failure of autologous hematopoietic stem cell transplantation (auto-HSCT) or after failure of at least two prior multi-agent chemotherapy regimens if not an auto-HSCT candidate *(see Appendix B);*
   b. As post-auto-HSCT consolidation if at high risk of relapse or progression;
   c. For previously untreated Stage III or IV cHL in combination with doxorubicin, vinblastine, and dacarbazine;
   d. Second-line therapy prior to HDT/ASCR to minimize the use of more intensive chemotherapy;

e. Palliative therapy as a single agent for relapsed or refractory disease in older adults (age > 60);

5. 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: 120 mg every 2 weeks;
      ii. All other indications: 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. Non-Hodgkin T-Cell Lymphomas (must meet all):

1. Diagnosis of one of the following (a, b, or c):
   a. A peripheral T-cell lymphoma (PTCL) (meets i and ii);
      i. Diagnosis of systemic anaplastic large cell lymphoma (sALCL);
      ii. Failure of at least one prior multi-agent chemotherapy regimen *(see Appendix B);*
   b. Breast implant-associated anaplastic large cell lymphoma (stage II - IV)*;*
   c. Adult T-cell leukemia/lymphoma (i or ii):
      i. Failure of at least one prior multi-agent chemotherapy regimen *(see Appendix B);*
      i. Subsequent therapy after high dose therapy/autologous stem cell rescue (HDT/ASCR);
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. sALCL: 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

C. Primary Cutaneous CD30+ T-cell Lymphoproliferative Disorder (must meet all):

1. Diagnosis of one of the following (a, b, or c):
   a. CD 30-positive pcALCL;
   b. Cutaneous ALCL with regional nodes *(excludes sALCL);*
   c. Lymphomatoid papulosis (LyP) with extensive lesions if relapsed/refractory to retreatment with primary treatment (e.g., methotrexate, phototherapy, systemic retinoids, topical steroids, or topical mechlorethamine [nitrogen mustard]), or retreatment with alternative regimen not used for primary treatment;
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. pcALCL: 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

D. Mycosis Fungoides/Sezary Syndrome (must meet all):
1. Diagnosis of one of CD30-expressing mycosis fungoides or Sezary syndrome;
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 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

E. 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): HIM.PHAR.21 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 covered indications 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 or ii):
      i. Previously untreated Stage III or IV cHL: 120 mg every 2 weeks;
      ii. All other indications: 1.8 mg/kg up to 180 mg every 3 weeks;
   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): HIM.PHAR.21 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 – HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
HDT/ASCR: high-dose therapy with autologous stem cell rescue
cHL: classical Hodgkin lymphoma
HSCT: hematopoietic stem cell transplantation
LyP: lymphomatoid papulosis
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

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine)	HL doxorubicin: 40 to 75 mg/m^2 IV every 21 to 28 days; bleomycin: 10 to 20 units/m^2 (0.25 to 0.5 units/kg) IV/IM/SC once or twice weekly; vinblastine: 3.7 mg/m^2 IV, titrated weekly to a maximum dose of 18.5 mg/m^2; dacarbazine: 375 mg/m^2 IV on day 1 (repeat every 15 days) or 150 mg/m^2/day IV for 5 days (may repeat every 4 weeks)	Varies per chemotherapy agent (see Dosing Regimen column)
Stanford V (doxorubicin, vinblastine, mechlorethamine , etoposide, vincristine, bleomycin, and prednisone)	HL doxorubicin: 40 to 75 mg/m^2 IV every 21 to 28 days; vinblastine: 3.7 mg/m^2 IV, titrated weekly to a maximum dose of 18.5 mg/m^2; mechlorethamine: total IV dose 0.4 mg/kg/course using dry ideal body weight, as single dose or may divide into 0.1 to 0.2 mg/kg daily doses; etoposide: 100 mg/m^2 IV bolus on days 1 to 3, repeat every 14 days for 3 cycles; vincristine: 1.4 mg/m^2/week IV; bleomycin: 10 to 20 units/m^2 (0.25 to 0.5 units/kg) IV/IM/SC once or twice weekly;	Varies per chemotherapy agent (see Dosing Regimen column)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	prednisone: 40 mg/m^2/day PO on days 1 through 14	
Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone)	HL bleomycin: 10 to 20 units/m^2 (0.25 to 0.5 units/kg) IV/IM/subQ once or twice weekly etoposide: 100 mg/m^2 IV bolus on days 1 to 3, repeat every 14 days for 3 cycles; doxorubicin: 40 to 75 mg/m^2 IV every 21 to 28 days; cyclophosphamide: 40-50 mg/kg IV in divided doses over 2 to 5 days OR 10-15 mg/kg IV every 7 to 10 days OR 3-5 mg/kg IV twice weekly; vincristine: 1.4 mg/m^2/week IV; procarbazine: 100 mg/m^2 PO on days 1-14; prednisone: 40 mg/m^2/day PO on days 1 through 14	Varies per chemotherapy agent (see Dosing Regimen column)
CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone)	sALCL cyclophosphamide: 40-50 mg/kg IV in divided doses over 2 to 5 days OR 10-15 mg/kg IV every 7 to 10 days OR 3-5 mg/kg IV twice weekly; doxorubicin: 40 to 75 mg/m^2 IV every 21 to 28 days; vincristine: 1.4 mg/m^2/week IV; prednisone: 5 to 60 mg PO QD	Varies per chemotherapy agent (see Dosing Regimen column)
CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone)	sALCL cyclophosphamide: 40-50 mg/kg IV in divided doses over 2 to 5 days OR 10-15 mg/kg IV every 7 to 10 days OR 3-5 mg/kg IV twice weekly; doxorubicin: 40 to 75 mg/m^2 IV every 21 to 28 days; vincristine: 1.4 mg/m^2/week IV; etoposide: 100 mg/m^2 IV bolus on days 1 to 3, repeat every 14 days for 3 cycles; prednisone: 5 to 60 mg PO QD	Varies per chemotherapy agent (see Dosing Regimen column)
Dose-adjusted EPOCH (etoposide, prednisone,	sALCL etoposide: 100 mg/m^2 IV bolus on days 1 to 3, repeat every 14 days for 3 cycles;	Varies per chemotherapy agent (see

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
vincristine, cyclophosphamide, and doxorubicin)	prednisone: 5 to 60 mg PO QD vincristine: 1.4 mg/m^2/week IV; cyclophosphamide: 40-50 mg/kg IV in divided doses over 2 to 5 days OR 10-15 mg/kg IV every 7 to 10 days OR 3-5 mg/kg IV twice weekly; doxorubicin: 40 to 75 mg/m^2 IV every 21 to 28 days	Dosing Regimen column)

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications
Not applicable

Appendix D: General Information

- While pcALCL and MF are FDA-approved as second-line therapies after prior systemic therapies, NCCN recommends both of these agents as first-line therapies in certain instances. Adcetris has an NCCN category 1 recommendation as first-line therapy for pcALCL and a 2a recommendation as first-line therapy for multiple subtypes of MF. Therefore, the pcALCL and MF coverage guidelines above do not require a prior trial of any systemic therapies.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
HL, sALCL, pcALCL, and MF	1.8 mg/kg up to 180 mg every 3 weeks as intravenous infusion over 30 minutes until disease progression or unacceptable toxicity. *For classical HL post-auto-HSCT consolidation treatment, initiate Adcetris treatment within 4–6 weeks post-auto-HSCT or upon recovery from auto-HSCT. These patients should continue treatment until a maximum of 16 cycles, disease progression, or unacceptable toxicity.*	180 mg every 3 weeks
Previously untreated Stage III or IV cHL	1.2 mg/kg up to 120 mg every 2 weeks as intravenous infusion	120 mg every 2 weeks

VI. Product Availability

Single-use vial: 50 mg for reconstitution

VII. References

1. Adcetris Prescribing Information. Bothell, WA: Seattle Genetics, Inc., Inc.; March 2018. Available at: http://adcetrisupdate.com/. Accessed April 30, 2018.
2. Brentuximab vedotin. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed December 11, 2017.
3. Hodgkin lymphoma (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed December 13, 2017.
4. T-cell lymphomas (Version 1.2018). In: National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed December 13, 2017.
5. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed December 13, 2017.

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

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.