

Clinical Policy: Brentuximab Vedotin (Adcetris)

Reference Number: CP.PHAR.303

Effective Date: 02/17

Last Review Date: 02/17

[Coding Implications](#)
[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for brentuximab vedotin (Adcetris®).

Policy/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 classical Hodgkin lymphoma (CHL);
2. Meets a or b:
 - a. FDA approved use, one of the following:
 - i. Treatment after failure of either of the following:
 - a) Autologous hematopoietic stem cell transplantation (auto-HSCT);
 - b) At least 2 prior multi-agent chemotherapy regimens if not an auto-HSCT candidate;
 - ii. As consolidation therapy following auto-HSCT if high risk for relapse/progression (high risk is defined as history of primary refractory disease or disease relapse < 12 months following primary treatment);
 - b. Off-label NCCN recommended use, one of the following:
 - i. Single agent second-line therapy prior to high-dose therapy with autologous stem cell rescue (HDT/ASCR) to minimize the use of more intensive chemotherapy;
 - ii. Single agent palliative therapy;
3. Member does not have either of the following:
 - a. Severe renal impairment (creatinine clearance [CrCl] < 30 mL/min);
 - b. Moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment;
4. No concomitant use of bleomycin.

**The WHO classification divides Hodgkin lymphoma (HL) into 2 main types: classical Hodgkin lymphoma (CHL) and nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL). CHL is characterized by the presence of Reed-Sternberg cells and accounts for 95% of HL in Western countries.*

Approval duration: 3 months

B. Anaplastic Large Cell Lymphoma* (must meet all):

1. Meets one of the following recommended uses (a or b):
 - a. FDA approved use (i and ii):

- i. Diagnosis of systemic (extra-cutaneous disease) anaplastic large cell lymphoma (sALCL);
 - ii. Failure of ≥ 1 prior multi-agent chemotherapy regimens;
 - b. Off-label NCCN recommended use (i, ii or iii):
 - i. Diagnosis of breast implant-associated ALCL (BI-ALCL);
 - a) Adcetris is prescribed as adjuvant systemic therapy for (1 or 2):
 - 1) Localized disease to capsule/implant/breast following incomplete excision/partial capsulectomy with residual disease;
 - 2) Extended disease (stages II - IV);
 - ii. Diagnosis of primary cutaneous ALCL (PC-ALCL) with multifocal lesions as (a or b):
 - a) Single-agent primary treatment;
 - b) Single agent treatment for relapsed/refractory disease;
 - iii. Diagnosis of cutaneous ALCL with regional nodes as (a or b):
 - a) Single-agent primary treatment;
 - b) Single agent treatment for relapsed/refractory disease;
2. Member does not have either of the following:
 - a. Severe renal impairment (creatinine clearance <30 mL/min);
 - b. Moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment;
3. No concomitant use of bleomycin.

**Classified under T-cell non-Hodgkin lymphoma.*

Approval duration: 3 months

C. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

1. The following NCCN recommended uses for Adcetris, meeting NCCN categories 1, 2a, or 2b, are approved per the CP.PHAR.57 Global Biopharm Policy:
 - a. Non-Hodgkin lymphoma:
 - i. Adult T-cell leukemia/lymphoma;
 - ii. AIDS-related B-cell lymphoma;
 - iii. Diffuse large B-cell lymphoma;
 - iv. Mycosis fungoides (MF)/Sezary syndrome (SS);
 - v. Peripheral T-cell lymphoma;
 - vi. Primary cutaneous CD30+ T-cell lymphoproliferative disorders.

II. Continued Approval

A. All Indications (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member has none of the following reasons to discontinue:
 - a. Disease progression or unacceptable toxicity;
 - b. Severe renal impairment (creatinine clearance <30 mL/min);
 - c. Moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment;
 - d. Concomitant use of bleomycin;
 - e. Grade 4* (life-threatening; urgent intervention indicated) peripheral neuropathy;

- f. Progressive multifocal leukoencephalopathy;
- g. Stevens-Johnson syndrome or toxic epidermal necrolysis.

**National Cancer Institute Common Toxicity Criteria for Adverse Events, version 4.0.*

Approval duration: 6 months

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

- 1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
- 2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

CD30 is a member of the tumor necrosis factor receptor family. CD30 is expressed on the surface of sALCL cells and on Hodgkin Reed-Sternberg (HRS) cells in CHL, and has limited expression on healthy tissue and cells. In vitro data suggest that signaling through CD30-CD30L binding may affect cell survival and proliferation. Brentuximab vedotin is an ADC. The antibody is a chimeric IgG1 directed against CD30. The small molecule, MMAE, is a microtubule disrupting agent. MMAE is covalently attached to the antibody via a linker. Nonclinical data suggest that the anticancer activity of Adcetris is due to the binding of the ADC to CD30-expressing cells, followed by internalization of the ADC-CD30 complex, and the release of MMAE via proteolytic cleavage. Binding of MMAE to tubulin disrupts the microtubule network within the cell, subsequently inducing cell cycle arrest and apoptotic death of the cells. Additionally, in vitro data provide evidence for antibody-dependent cellular phagocytosis (ADCP).

Formulations:

Adcetris (brentuximab vedotin) for Injection is supplied as a lyophilized cake or powder for reconstitution.

- Each single-use vial contains 50 mg brentuximab vedotin

FDA Approved Indications:

Adcetris is a CD30-directed antibody-drug conjugate/intravenous formulation indicated for:

- CHL
 - Treatment of patients with 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.
- CHL post-auto-HSCT consolidation
 - Treatment of patients with CHL at high risk of relapse or progression as post-auto-HSCT consolidation.
- sALCL
 - Treatment of patients with sALCL after failure of at least one prior multi-agent chemotherapy regimen. The sALCL indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may

be contingent upon verification and description of clinical benefit in confirmatory trials.

Appendices

Appendix A: Abbreviation Key

ADCP: Antibody-dependent cellular phagocytosis	HSCT: Hematopoietic stem cell transplantation
ALCL: Anaplastic large cell lymphoma	MF: Mycosis fungoides
BI-ALCL: Breast implant-associated anaplastic large cell lymphoma	NLPHL: Nodular lymphocyte-predominant Hodgkin lymphoma
HDT/ASCR: High-dose therapy with autologous stem cell rescue	PC-ALCL: Primary cutaneous anaplastic large cell lymphoma
CHL: Classical Hodgkin lymphoma	sALCL: Systemic anaplastic large cell lymphoma
HL: Hodgkin lymphoma	SS: Sezary syndrome
HRS: Hodgkin Reed-Sternberg	

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	Approval Date
Policy split from CP.PHAR.182 Excellus Oncology.	01/17	02/17

References

1. Adcetris prescribing information. Bothell, WA: Seattle Genetics, Inc.; September 2016. Available at <https://adcetris.com/pdf/ADCETRIS-brentuximab-vedotin-Prescribing-Information.pdf?v=20161101>. Accessed January 11, 2017.
2. Brentuximab vedotin. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed January 11, 2017.
3. Hodgkin lymphoma (Version 3.2016). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed January 12, 2017.
4. T-cell lymphomas (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed January 12, 2017.
5. Freedman AS, Aster JC. Clinical manifestations, pathologic features, and diagnosis of systemic anaplastic large cell lymphoma. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed January 12, 2016.

Important Reminder

CLINICAL POLICY

Brentuximab Vedotin



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.

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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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs and LCDs, and

CLINICAL POLICY

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Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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