Clinical Policy: Brentuximab Vedotin (Adcetris)

Reference Number: PA.CP.PHAR.303
Effective Date: 01/2018
Last Review Date: 08/2025

Description
Brentuximab vedotin for injection (Adcetris®) is a CD30-directed antibody and microtubule inhibitor 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
- B-cell lymphoma:
  - Relapsed or refractory large B-cell lymphoma (LBCL), 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 eligible for auto-HSCT or chimeric antigen receptor (CAR) T-cell therapy, in combination with lenalidomide and a rituximab product

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

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

Policy/Criteria
It is the policy of PA Health & Wellness ® 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 classical Hodgkin lymphoma (cHL);
2. Prescribed by or in consultation with an oncologist or hematologist;

3. Age ≥ 18 years;
   ** If the age is between 2 to 39 years, consider using criteria B below for cHL in Pediatric and Adolescent Patients*
4. If previously untreated disease, prescribed in one of the following ways (a-d):
   a. In combination with AVD (doxorubicin, vinblastine, and dacarbazine);
      †If vinblastine is unavailable due to shortage, may be prescribed in combination with CHP (cyclophosphamide, doxorubicin, prednisone) instead
   b. For age > 60 years: In combination with dacarbazine or nivolumab;
   c. For age 18-61 years OR Deauville score 4-5: As a component of BrECADD (brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone) with granulocyte colony-stimulating factor;
   d. Other category 1, 2A, or 2B NCCN-recommended uses not listed;
5. If relapsed 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*).

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 ≥ 2 years to 39 years;
4. One of the following (a-d):
   a. If previously untreated: Prescribed as a component of one of the following (i-iv):
      i. Bv-AVE-PC (brentuximab vedotin, doxorubicin, vincristine, etoposide, prednisone, cyclophosphamide);
      ii. AEPA (brentuximab vedotin, etoposide, prednisone, doxorubicin);
      iii. Stage III-IV disease only: Bv-AVD (brentuximab vedotin, doxorubicin, vinblastine, dacarbazine);
      iv. Stage III-IV disease only: BrECADD (brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone);
   b. If following AEPA: Prescribed as a component of CAPDAC (cyclophosphamide, brentuximab vedotin, prednisone, dacarbazine);
   c. For relapsed or refracory disease (i, ii or iii):
      i. Prescribed in combination with involved-site radiation therapy (ISRT);

ii. Prescribed in combination with bendamustine, nivolumab, or gemcitabine;
iii. Prescribed following high-dose therapy and autologous stem cell rescue for high-risk disease (progressive disease, refractory disease, or relapse within 1 year of original diagnosis);

d. Other category 1, 2A, or 2B NCCN-recommended uses not listed;

5. If request is for stage I-II disease, member has risk factors (*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*).

Approval duration: 6 months

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

1. Diagnosis of one of the following (a-f):
   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 peripheral T-cell lymphoma 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 (off-label);
   f. Other category 1, 2A, or 2B NCCN recommended uses;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Prescribed in one of the following ways (a-d)
   a. As a single agent;
   b. In combination with CHP (cyclophosphamide, doxorubicin, prednisone);
   c. For PTCL, breast implant-associated ALCL, or hepatosplenic T-cell lymphoma only: In combination with bendamustine for relapsed/refractory disease;
   d. Other category 1, 2A, or 2B NCCN-recommended uses not listed;
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

D. Primary Cutaneous CD30+ T-cell Lymphoproliferative Disorder (must meet all):
1. Diagnosis of one of the following (a-d):
   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);
   d. Other NCCN recommendations listed as category 1, 2A, or 2B;
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)*.

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)*.

Approval duration: 6 months

F. B-Cell Lymphomas (must meet all)**:**
1. Diagnosis of one of the following (a-f):
   a. LBCL
   b. Diffuse large B-cell lymphoma (DLBCL);
   c. High-grade B-cell lymphoma (HGBL);
   d. HIV-related B-cell lymphoma (off-label);
   e. Post-transplant lymphoproliferative disorder (PTLD) (B-cell type) (off-label);
   f. Other category 1, 2A, or 2B NCCN-recommended uses not listed;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Prescribed in one of the following (a,b or c):
   a. Age ≥ 18 years and is prescribed in one of the following ways (i, ii or iii):
      i. In combination with lenalidomide and rituximab;
      ii. In combination with nivolumab (off-label);
      iii. As a single agent (off-label);
   b. Age < 18 years (off-label) and both of the following (i and ii):
      i. Disease is primary mediastinal LBCL;
      ii. Prescribed in combination with nivolumab or pembrolizumab;
   c. Other NCCN recommendations listed as category 1, 2A, or 2B;

4. Adcetris is prescribed as subsequent therapy;
5. One of the following (a or b):
   a. Member is not a candidate or no intention to proceed to allogeneic, autologous stem cell transplant, or CAR T-cell therapy;
   b. Other category 1, 2A, or 2B NCCN-recommended uses not listed;
6. Except for HIV-Related B-Cell Lymphomas and histologic transformation of indolent lymphomas to diffuse large B-Cell Lymphomas, disease is relapsed, progressive or refractory or has had a partial response;
7. For HIV-Related B-Cell Lymphomas, used as second or third-line and subsequent therapy or has relapsed plasmablastic lymphoma;
8. Request meets one of the following (a or b):
   a. LBCL: Dose does not exceed 1.2 mg/kg up to 120 mg every 3 weeks;
   b. 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

G. Other diagnoses/indications

1. Refer to the PA.CP.PMN.53 for Medicaid.

II. Continued Approval

A. All Indications (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.PHARM.01) applies;;
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-ix):
      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;
      ix. LBCL: 1.2 mg/kg up to 120 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 PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies; or
2. Refer to PA.CP.PMN.53

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 – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CAR: chimeric antigen receptor
cHL: classical Hodgkin lymphoma
DLBCL: disffuse large B-cell lymphoma
FDA: Food and Drug Administration
HGBL: high-grade B-cell lymphoma
HSCT: hematopoietic stem cell transplantation
LBCL: large B-cell lymphoma
ISRT: involved-site radiation therapy
MF: mycosis fungoides
NCCN: National Comprehensive Cancer Network
NOS: not otherwise specified
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: Risk Factors for Pediatric cHL

Per NCCN, risk factors for pediatric cHL, defined by EuroNET-PHL and Children's Oncolog Group (COG), include:

- Erythrocyte sedimentation rate (ESR) > 30 mm/h
- B symptoms (unexplained recurrent fever > 38°C within the last month; drenching night sweats; or weight loss > 10% of body weight within 6 months of diagnosis)
- Mediastinal mass with mediastinal mass ratio (MMR) > 0.33
- Any E lesions, defined as a contiguous infiltration of a lymph node mass into extralymphatic structures or organs (e.g., lung or bone)
    - Pleural and pericardial involvement should be considered E-lesions, but a pleural or pericardial effusion alone is not considered an E-lesion. Disease that extends beyond the lymphatic system without adjacent lymphatic involvement is considered stage IV;

liver or bone marrow involvement is always considered stage IV disease. CNS disease is considered extra-axial

- Bulky with contiguous tumor volume > 200 mL or > 6 cm extra-mediastinal nodal conglomerate

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
Relapsed or refractory LBCL	1.2 mg/kg up to a maximum of 120 mg in combination with lenalidomide and rituximab. Administer every 3 weeks until disease progression, or unacceptable toxicity	120 mg every 3 weeks

VI. Product Availability

Single-use vial: 50 mg for reconstitution

VII. References

1. Adcetris Prescribing Information. Bothell, WA: Seagen, Inc.; February 2025. Available at: https://www.adcetris.com/. Accessed April 14, 2025.
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 April 21, 2025.
4. National Comprehensive Cancer Network. Hodgkin Lymphoma Version 2.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf. Accessed May 6, 2025.
5. National Comprehensive Cancer Network.Pediatric Hodgkin Lymphoma Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_hodgkin.pdf. Accessed May 6, 2025.
6. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version 2.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed May 6, 2025.
7. National Comprehensive Cancer Network. T-Cell Lymphomas Version 1.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed May 6, 2025.
8. National Comprehensive Cancer Network. B-Cell Lymphomas Version 2.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed May 6, 2025.

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
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.	04/2018
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/2019
Q3 2020 annual review: updated Non-Hodgkin T-Cell Lymphomas criteria set to allow use as first-line therapy for PTCL to align with updated FDA-approved indication; NCCN and FDA-approved uses summarized for clarity; 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; NCCN recommended uses added - B-cell lymphomas, additional T-	07/2020

Reviews, Revisions, and Approvals	Date
cell lymphomas; 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.	
3Q 2021 annual review: no significant changes; references reviewed and updated.	07/2021
3Q 2022 annual review: per NCCN Compendium clarified extranodal NK/T-cell lymphoma should be in the relapsed or refractory setting and removed requirement for nasal type; clarified hepatosplenic T-cell lymphoma should be after two first-line therapy regimens; references reviewed and updated.	07/2022
RT4: New indication of previously untreated high risk cHL in pediatric and adolescent patients added to policy	01/2023
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.	07/2023
3Q 2024 annual review: per NCCN – for cHL, added pathway for use as a component of BrECADD for stage III-IV disease for members aged 18-61 years; for T-cell lymphomas, removed requirement for 2 prior therapies for hepatosplenic T-cell lymphoma and added pathway for combination use with bendamustine for PTCL, breast implant-associated ALCL, and hepatosplenic T-cell lymphoma; for MF and Sezary syndrome, added that Adcetris must be prescribed as a single agent, in combination with skin-directed therapy, or in combination with bendamustine; for B-cell lymphomas, removed T-cell type monomorphic PTLD; references reviewed and updated.	07/2024
RT4: added criteria for new FDA-approved indication of relapsed or refractory LBCL in adult patients – added criterion that disease is relapsed or refractory, added option that member is not a candidate for CAR T-cell therapy; per NCCN for B-cell lymphomas – added pathway for off-label use as a single agent or in combination with rituximab or nivolumab, clarified use in HIV-related B-cell lymphoma and PTLD are off-label indications.	04/2025
3Q 2025 annual review: per NCCN – for cHL, added option for use with CHP as alternative to AVD if vinblastine is unavailable due to shortage, added	07/2025

Reviews, Revisions, and Approvals	Date
option for use with nivolumab for age > 60 years, revised requirements around use as component of BrECADD (removed requirement for stage III-IV disease, added option for use with Deauville score 4-5, added requirement for use with granulocyte colony-stimulating factor); for pediatric cHL, added option for use as a component of BrECADD and Bv-AVD for stage III-IV disease, specified that only use following high-dose therapy and autologous stem cell rescue has to be in high-risk disease, and modified requirement for high risk disease for nearly all requests to instead require risk factors only for stage I-II disease; references reviewed and updated.	