Clinical Policy: Brentuximab Vedotin (Adcetris)

Reference Number: PA.CP.PHAR.303
Effective Date: 01/2018 Coding Implications
Last Review Date: 07/2023

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 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 or b):
   a. In combination with AVD (doxorubicin, vinblastine, and dacarbazine);
   b. For age > 60 years: In combination with dacarbazine;
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, 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, 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;
5. For all requests except when prescribed in combination with ISRT or bendamustine, nivolumab, or 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*).

Approval duration: 6 months

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

1. Diagnosis of one of the following (a, b, c, d, e or 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 after two first-line therapy regimens (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. 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*).

Approval duration: 6 months

D. Primary Cutaneous CD30+ T-cell Lymphoproliferative Disorder (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).*

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 (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, except for primary mediastinal large B-cell lymphoma or pediatric mediastinal large B-cell lymphoma;
5. For subtypes other than monomorphic PTLD (T-cell type) or primary or pediatric mediastinal large B-cell lymphoma, 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*).

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.LTSS.PHAR.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, 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*).

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.LTSS.PHAR.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

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: Definition of High Risk Disease

Bulk disease is defined as:
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-	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

expressing MF in adults		

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 2.2022. 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 1.2022. 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 1.2022. 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 2.2022. 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 3.2022. 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	Approval 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	

Reviews, Revisions, and Approvals	Date	Approval Date
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-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.	07/2020	
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	