Clinical Policy: Brentuximab Vedotin (Adcetris)

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

Coding Implications

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. 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

A. Classical Hodgkin Lymphoma in Pediatric and Adolescent Patients (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Previously untreated pathologically confirmed cHL meeting one of the following Ann Arbor stages (i, ii,ii or vi):
      i. Stage IIB with bulk tumor (*see Appendix D for the definition of Bulk Disease*);
      ii. Stage IIIB;
      iii. Stage IVA;
      vi. Stage IVB;
   b. NCCN category 1, 2A or 2B recommendation;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 2 years to 39 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 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

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

1. Diagnosis of one of the following (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 (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);
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 Disorder (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. 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

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, b, c, or d):
   a. Diffuse large B-cell lymphoma, including but not limited to (i, ii, or iii):
      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;
      iii. Primary mediastinal large B-cell lymphoma;
   b. High-grade B-cell lymphoma;
   c. AIDS-related B-cell lymphoma;
   d. Post-transplant lymphoproliferative disorder - monomorphic PTLD (T-cell type);
2. Prescribed by or in consultation with an oncologist or hematologist;

3. Age ≥ 18 years [except for pediatric aggressive mature B-cell lymphomas (primary mediastinal large B-cell lymphoma)];
4. Disease is CD30-positive;
5. For subtypes other than monomorphic PTLD (T-cell type), 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 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, or vii):
      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
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 Bulk Disease

Bulk disease is defined as:

- 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;
- 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).

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	180 mg every 3 weeks up to 16 cycles

	3 weeks until a maximum of 16 cycles, disease progression, or unacceptable toxicity.	
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

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 November 30, 2022.
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 2, 2022.
4. National Comprehensive Cancer Network. Hodgkin Lymphoma Version 2.2022. Available at https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf. Accessed May 2, 2022.
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 2, 2022.
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 2, 2022.
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 2, 2022.
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 2, 2022.

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	
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	