Clinical Policy: Brentuximab Vedotin (Adcetris)

Reference Number: PA.CP.PHAR.303
Effective Date: 01/18
Last Review Date: 07/17/19

Coding Implications
Revision Log

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

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
It is the policy of Pennsylvania Health and Wellness ® 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. 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. 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. 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 PA.CP.PMN.53 for Medicaid.

II. Continued Approval

A. All Indications (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and 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 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 Pennsylvania Health and 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

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 reconstititon.

- Each single-use vial contains 50 mg brentuximab vedotin

III. Appendices

Appendix A: Abbreviation Key

ADCP: Antibody-dependent cellular phagocytosis
ALCL: Anaplastic large cell lymphoma
BI-ALCL: Breast implant-associated anaplastic large cell lymphoma
HDT/ASCR: High-dose therapy with autologous stem cell rescue
CHL: Classical Hodgkin lymphoma
HL: Hodgkin lymphoma
HRS: Hodgkin Reed-Sternberg
HSCT: Hematopoietic stem cell transplantation
MF: Mycosis fungoides
NLPHL: Nodular lymphocyte-predominant Hodgkin lymphoma
PC-ALCL: Primary cutaneous anaplastic large cell lymphoma
sALCL: Systemic anaplastic 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;	Varies per chemotherapy agent (see Dosing Regimen column)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	bleomycin: 10 to 20 units/m^2 (0.25 to 0.5 units/kg) IV/IM/SC once or twice weekly; 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)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin)	sALCL 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 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	Varies per chemotherapy agent (see 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.

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.	04.18	

Reviews, Revisions, and Approvals	Date	Approval Date
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/17/19	

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.