Clinical Policy: Brentuximab Vedotin (Adcetris)

Reference Number: PA.CP.PHAR.303
Effective Date: 01/18
Last Review Date: 11/17

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®).

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. 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, disease relapse < 12 months following primary treatment, or disease relapse > 12 months with extranodal disease);
   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 PA.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 PA.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 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 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 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.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 reconstititon.
- 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
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

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

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.