I. PURPOSE
To define and describe the accepted indications for Adcetris (brentuximab vedotin) usage in the treatment of cancer.

II. DEFINITIONS

Adcetris (brentuximab vedotin): is a CD30-directed antibody-drug conjugate (ADC) consisting of 3 components: the chimeric IgG1 antibody cAC10 which is specific for human CD30; the microtubule disrupting agent MMAE; and a protease-cleavable linker that covalently attaches MMAE to cAC10. The anticancer activity of brentuximab vedotin is presumed to be 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. The microtubule disrupting agent MMAE binds to tubulin, disrupting the microtubule network which leads to cell cycle arrest and apoptotic death of the cells.

Adcetris (brentuximab vedotin) is FDA approved for the treatment of members with Hodgkin lymphoma: (1) after failure of autologous stem cell transplant (ASCT) or after failure of at least two prior multiagent chemotherapy regimens in patients who are not ASCT candidates, (2) for the treatment of adult patients with cHL at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation, (3) for the treatment of patients with systemic anaplastic large cell lymphoma after failure of at least one prior multiagent chemotherapy regimen, (4) for the treatment of previously untreated Stage III or IV cHL, in combination with chemotherapy, (5) for the treatment of adult patients with pcALCL or CD30-expressing MF who have received prior systemic therapy, and (6) 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.

Adcetris (brentuximab vedotin) is available as an intravenous powder for solution: 50 mg.

III. POLICY
New Century is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.
Inclusion Criteria: Adcetris (brentuximab vedotin) may be considered medically necessary when any of the following selection criteria is met:

1. Classical Hodgkin Lymphoma
   a. Adcetris (brentuximab vedotin) is being used in member with classical Hodgkin Lymphoma that is CD30 positive and the following:
      i. Primary treatment in combination with dacarbazine for stage I-II unfavorable or stage III-IV disease OR in combination with AVD (doxorubicin, vinblastine, dacarbazine) for stage III-IV disease OR
      ii. After failure of ASCT (autologous stem cell transplant) OR
   III. After failure of at least two prior multi-agent chemotherapy regimens in members who are not ASCT candidates OR
   iv. As maintenance therapy following high-dose therapy and autologous stem cell rescue for primary refractory or extranodal disease or relapse <12 months following primary therapy in patients who have not received prior brentuximab vedotin AND
   v. Weight calculation, for dosage, not to exceed 100kg which translates to no more than 180mg per dose.

2. Non Hodgkin Lymphoma
   a. Adcetris (brentuximab vedotin) is being used as in member with Systemic Anaplastic Large Cell Lymphoma (ALCL) that is CD30 positive and the following:
      i. After failure of at least one prior multiagent chemotherapy regimen AND
      ii. Weight calculation, for dosage, not to exceed 100kg which translates to no more than 180mg per dose.
   b. Therapy for primary cutaneous anaplastic large cell lymphoma (ALCL) as primary or relapsed/refractory disease.

3. Peripheral T-Cell Lymphomas (PTCL)
   a. Adcetris (brentuximab vedotin) is being used for PTCL that is CD30 positive and any of the following:
      i. First line therapy as a component of brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, prednisone) OR
      iii. Second line or subsequent therapy as a single agent for relapsed/refractory disease.

Exclusion Criteria: Adcetris (brentuximab vedotin) is not considered medically necessary when any of the following selection criteria is met:

1. Disease progression while on Adcetris (brentuximab vedotin).
2. Avoid use in severe renal impairment (creatinine clearance less than 30 mL/min) or moderate to severe hepatic impairment (Child-Pugh B or C).
3. Dosing exceeds single dose limit of Adcetris (brentuximab vedotin) 180 mg (1.8 mg/kg/dose) or 120 mg (1.2 mg/kg/dose).
4. Treatment with Adcetris (brentuximab vedotin) exceeds the maximum duration limit of 16 cycles (12 doses for first line treatment of Hodgkin's Disease.)
5. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Adcetris (brentuximab vedotin) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. Dosage and Administration:
   a. Hodgkin's disease Refractory or Consolidation therapy/ MF/ALCL: 1.8 mg/kg administered only as an intravenous infusion over 30 minutes every 3 weeks, not exceed 180 mg per dose. Do not administer as an intravenous push or bolus. Continue treatment until a maximum of 16 cycles, disease progression or unacceptable toxicity.
   b. Hodgkin's disease, First-line treatment: 1.2 mg/kg IV infusion over 30 minutes every 2 weeks; max dose 120 mg; Max duration 12 doses, disease progression, or unacceptable toxicity.
   c. Previously untreated PTCL in combination with chemotherapy: 1.8 mg/kg up to a maximum of 180 mg every 3 weeks for 6 to 8 doses.

2. Dosage Adjustments:
   a. Renal impairment, mild or moderate (CrCl 30 to 80 mL/min): No dosage adjustment required.
   b. Renal impairment, severe (CrCl less than 30 mL/min): Avoid use.
   c. Hepatic impairment, mild (Child-Pugh A) and usual dosage is 1.8 mg/kg: Reduce dose to 1.2 mg/kg (maximum, 120 mg).
   d. Hepatic impairment, mild (Child-Pugh A) and usual dosage is 1.2 mg/kg: Reduce dose to 0.9 mg/kg (maximum, 90 mg).
   e. Hepatic impairment, moderate to severe (Child-Pugh B or C): Avoid use.
   f. Neutropenia, grade 3 or 4 and usual dosage is 1.8 mg/kg: withhold dose until resolved to baseline or grade 2 or lower; consider growth factor support for subsequent cycles; for grade 4 despite growth factors, discontinue or reduce dose to 1.2 mg/kg.
   g. Neutropenia, grade 3 or 4 and usual dosage is 1.2 mg/kg: Administer granulocyte-colony stimulating factor prophylaxis for subsequent cycles for patients not receiving primary G-CSF prophylaxis.
   h. Peripheral neuropathy, grade 2 or 3 (new or worsening) and usual dosage is 1.8 mg/kg : withhold dose until improved to baseline or grade 1, then restart at 1.2 mg/kg
   i. Peripheral neuropathy, grade 2 and usual dosage is 1.2 mg/kg : reduce dosage to 0.9 mg/kg (max 90 mg) every 2 weeks
   j. Peripheral neuropathy, grade 3 and usual dosage is 1.8 mg/kg : withhold dose until improved to baseline or grade 1, then restart at 1.2 mg/kg
   k. Peripheral neuropathy, grade 4: discontinue.

3. Monitoring
   a. A complete or partial response determined by clinical and radiographic measures indicates efficacy.
b. Prior to each dose, assess CBC, including differential.
c. Observe patients for infusion-related reactions, including anaphylaxis.
d. Monitor patients for signs of tumor lysis syndrome, especially those with highly proliferative tumors or high tumor burden prior to treatment.
e. Monitor patients for symptoms of peripheral neuropathy, such as hypoesthesia, hyperesthesia, paresthesia, discomfort, burning sensation, neuropathic pain or weakness.
f. Progressive multifocal leukoencephalopathy (PML) resulting from John Cunningham (JC) virus, including fatal cases have been reported; discontinue therapy if PML is confirmed.
g. Concomitant use of ADCETRIS and bleomycin is contraindicated due to pulmonary toxicity. In a clinical trial that studied ADCETRIS with bleomycin as part of a combination regimen, the rate of non-infectious pulmonary toxicity was higher than the historical incidence reported with ABVD (adriamycin, bleomycin, vinblastine, dacarbazine). Patients typically reported cough and dyspnea. Interstitial infiltration and/or inflammation were observed on radiographs and computed tomographic imaging of the chest. Most patients responded to corticosteroids.

V. APPROVAL AUTHORITY
   1. Review – UM Department
   2. Final Approval – UM Committee

VI. ATTACHMENTS
   None

VII. REFERENCES