



Original Effective Date: 12/01/2018
 Current Effective Date: 03/18/2023
 Last P&T Approval/Version: 01/25/2023
 Next Review Due By: 01/2024
 Policy Number: C15428-A

Adcetris (brentuximab vedotin)

PRODUCTS AFFECTED

Adcetris (brentuximab vedotin)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:

Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:

Classical Hodgkin lymphoma (cHL), systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF)

NOTE: Patient's must have a documented diagnosis for a medically accepted indication including: Use of a drug which is FDA-approved. Use of which is supported by one or more citations included or approved for inclusion in any of the compendia: American Hospital Formulary Service Drug Information, DRUGDEX Information System, National Comprehensive Cancer Network (categories 1 or 2A only).

(NOTE: A category 2B therapy/regimen may be authorized on an exception basis with documented Molina Healthcare medical director or Molina Healthcare oncologist consultation)

REQUIRED MEDICAL INFORMATION:

This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for

Drug and Biologic Coverage Criteria
adequate review.

A. CLASSICAL HODGKIN LYMPHOMA:

1. Diagnosis of classical Hodgkin lymphoma (cHL)
AND
 2. Documentation member meets ANY of the following conditions:
 - (a) Previous failure of autologous hematopoietic stem cell transplant (auto-HSCT) for treatment of cHL
OR
 - (b) Relapsed disease after failure of at least two (2) prior multi-agent chemotherapy regimens in member who is not an auto-HSCT candidate
OR
 - (c) Consolidation/Maintenance therapy following an autologous hematopoietic stem cell transplant in patients at high risk for relapse or progression AND ONE of the following conditions defining high risk: (i) Disease was refractory to primary therapy, (ii) Disease relapsed in less than 12 months of primary therapy OR (iii) Disease with extra nodal involvement prior to auto- HSCT
OR
 - (d) Second-line therapy prior to high-dose therapy and autologous stem cell rescue (HDT/ASCR) to minimize the use of more intensive chemotherapy
OR
 - (e) Palliative therapy as a single agent for relapsed or refractory disease in older adults (age >60)
OR
 - (f) Treatment for Stage I-II unfavorable disease in older adult (age > 60)
OR
 - (g) For previously untreated Stage III or IV cHL, in combination with chemotherapy [doxorubicin, vinblastine, and dacarbazine] Documentation of ONE of the following:
 - (a) Prescriber attests that member has no known neuropathy AND Member has an International Prognostic Score (IPS) ≥ 4
OR
 - (b) Member has a labeled medical contraindication to bleomycin-based therapy (ABVD)
OR
 - (c) Brentuximab is considered medically necessary to reduce the risk of bleomycin pulmonary toxicity in cycles 3-6: after 4 doses/2 cycles with bleomycin, and a PET/CT showing Deauville of 4-5 requiring escalation in therapy, and on a case-by-case basis, for individuals for whom there is expressed concern for the development of bleomycin pulmonary toxicity with further treatment (i.e., Medical reasons for why the recommended alternative Escalated BEACOPP cannot be used).
NOTE: the proper succession for these criteria can be found within compendia monographs, FDA label or NCCN guidelines; If compendia monographs, FDA label or NCCN guidelines have a formulary/preferred product at therapeutic parity with requested agent a formulary/preferred product should be used first where state regulations allow. Molina reviewers and delegates will comply with all regulations and requirements applicable to the review of the request, providing exception to our standard criteria as may be required under state regulations and requirements.
 - (h) For previously untreated high risk cHL in combination with chemotherapy [doxorubicin, vincristine, etoposide, prednisone, and cyclophosphamide]
- AND
3. Documentation of member's current weight (within the last 30 days)

Drug and Biologic Coverage Criteria

B. ALL OTHER LABELED INDICATIONS:

1. (a) Prescribed as a SINGLE agent for relapsed or refractory disease for ONE of the following diagnoses: Systemic Anaplastic Large Cell Lymphoma (sALCL), CD30+ Peripheral T-Cell Lymphoma (PTCL), CD30+ angioimmunoblastic T-cell lymphoma (AITL)
AND
(b) Documentation of failure of at least one prior multi-agent chemotherapy regimen
OR
2. Prescribed in combination with cyclophosphamide, doxorubicin, and prednisone for previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30- expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma (AITL) and PTCL not otherwise specified
AND
3. (a) Prescribed for CD30+ adult T-cell leukemia/lymphoma
AND
(b) Failure of at least one prior multi-agent chemotherapy regimen OR Subsequent therapy after high-dose therapy and autologous stem cell rescue (HDT/ASCR) OR Initial therapy in combination with cyclophosphamide, doxorubicin, and prednisone
OR
4. (a) Prescribed as adjuvant systemic therapy for breast implant-associated ALCL localized disease to capsule/implant/breast AND Member had incomplete excision or partial capsulectomy with residual disease
OR
(b) Member has breast implant-associated ALCL extended disease (stage II-IV)
OR
5. Diagnosis of CD30-expressing mycosis fungoides or Sezary syndrome
OR
6. Prescribed as a single agent for ONE of the following diagnosis: CD 30+ primary cutaneous anaplastic large cell lymphoma (pcALCL), OR Cutaneous anaplastic large cell lymphoma (ALCL) with regional nodes (excludes sALCL) OR Lymphomatoid papulosis (LyP) with extensive lesions if refractory to all primary treatment options
OR
7. Prescribed as second line therapy for diffuse large B cell lymphoma for CD30+ disease in a member who is not a candidate for transplant
AND
8. Documentation of member's current weight (within the last 30 days)

C. OFF-LABEL USE: Refer to the 'Off-Label Use of Drugs and Biologic Agents' if diagnosis is NOT specifically listed above.

CONTINUATION OF THERAPY:

A. FOR ALL INDICATIONS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
AND
2. Documented clinically significant improvements in the disease state, stability on the medication, or lack of disease progression
AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
4. Documentation of member's current weight (within the last 30 days)

Drug and Biologic Coverage Criteria

DURATION OF APPROVAL:

Initial authorization: 3 months, Continuation of therapy: 6 months or maximum duration per FDA label or NCCN guideline, whichever is shorter

PRESCRIBER REQUIREMENTS:

Prescribed by, or in consultation with, a board-certified hematologist/oncologist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

High risk classical Hodgkin lymphoma: 2 years of age and older
All other indications: 18 years of age and older

QUANTITY:

Hodgkin lymphoma, advanced (Stage III or IV), previously untreated: 1.2 mg/kg (maximum dose: 120 mg) every 2 weeks until a maximum of 12 doses
Pediatric Hodgkin lymphoma, high risk, previously untreated: 1.8 mg/kg (maximum dose: 180 mg) every 3 weeks until a maximum of 5 doses
Hodgkin lymphoma relapsed or refractory: 1.8 mg/kg (maximum dose: 180 mg) every 3 weeks
Hodgkin lymphoma, consolidation therapy after autologous hematopoietic stem cell transplantation (HSCT): 1.8 mg/kg (maximum dose: 180 mg) every 3 weeks until a maximum of 16 cycles
Mycosis fungoides (CD-30 expressing): 1.8 mg/kg (maximum dose: 180 mg) every 3 weeks, continue until a maximum of 16 cycles
Primary cutaneous anaplastic large cell lymphoma, relapsed (pcALCL): 1.8 mg/kg (maximum dose: 180 mg) every 3 weeks, continue until a maximum of 16 cycles
Peripheral T-cell lymphoma (CD30-expressing), previously untreated: IV: 1.8 mg/kg (maximum dose: 180 mg) every 3 weeks for 6 to 8 doses (in combination with cyclophosphamide, doxorubicin, and prednisone). Administer primary prophylaxis with G-CSF (filgrastim) beginning with cycle 1.
Systemic anaplastic large cell lymphoma, previously untreated: 1.8 mg/kg (maximum dose: 180 mg) every 3 weeks for 6 to 8 doses (in combination with cyclophosphamide, doxorubicin, and prednisone)
Systemic anaplastic large cell lymphoma, relapsed: IV: 1.8 mg/kg (maximum dose: 180 mg) every 3 weeks
Adult T-Cell Leukemia/Lymphoma, initial therapy: 1.8 mg/kg (maximum dose: 180 mg) every 3 weeks for 6 to 8 doses (in combination with cyclophosphamide, doxorubicin, and prednisone).
Adult T-Cell Leukemia/Lymphoma, second line or subsequent therapy: 1.8 mg/kg (maximum dose: 180 mg) every 3 weeks
Diffuse large B cell lymphoma (DLBCL) with CD30+ expression, relapsed/refractory: 1.8 mg/kg (maximum dose: 180 mg) every 3 weeks

Maximum Quantity Limits – << based on FDA label >>

PLACE OF ADMINISTRATION:

The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-inpatient hospital facility-based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Intravenous

DRUG CLASS:

Antineoplastic Antibody-Drug Complexes

FDA-APPROVED USES:

Adcetris (brentuximab vedotin) is indicated for treatment of:

Drug and Biologic Coverage Criteria

- Adult patients with previously untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine
- Pediatric patients 2 years and older with previously untreated high risk classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vincristine, etoposide, prednisone, and cyclophosphamide
- Adult patients with classical Hodgkin lymphoma (cHL) at high risk of relapse or progression as post autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation
- Adult patients with classical Hodgkin lymphoma (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
- Adult patients with 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
- Adult patients with systemic anaplastic large cell lymphoma (sALCL) after failure of at least one prior multiagent chemotherapy regimen
- Adult patients with primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) who have received prior systemic therapy

COMPENDIAL APPROVED OFF-LABELED USES:

None

APPENDIX

APPENDIX:

None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Lymphoma is a general term for a group of cancers that originate in the lymphatic system. There are two major subgroups of lymphoma, Hodgkin lymphoma (HL) and non-Hodgkin lymphoma; both express CD30. NHL is divided into two major subgroups, based on the appearance and immunophenotype of the tumor cells: Nodular lymphocyte predominant HL and Classic HL. Classical HL is a type of Hodgkin lymphoma characterized by an abnormal type of B lymphocyte called Reed Sternberg cells. It accounts for 90 to 95 percent of Hodgkin lymphoma. The National Cancer Institute estimates that there will be 8,500 new cases of Hodgkin lymphoma and an estimated 1,050 deaths in 2018. The treatment of patients with Hodgkin lymphoma is primarily guided by the clinical stage of disease. Brentuximab combines the action of an antibody with chemotherapy (an antibody-drug conjugate). An antibody-drug conjugate designed to target tumor cells expressing CD30, a tumor necrosis factor (TNF) receptor. The antibody-drug conjugate binds with the CD30, and a small molecule chemotherapeutic agent (monomethyl auristatin [MMAE]) is released. The MMAE causes cell cycle arrest and cell death. Indicated for the treatment of patients with:

- 1) Classical Hodgkin lymphoma (HL) after failure of autologous stem cell transplant (ASCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not ASCT candidates,
- 2) Classical HL at high risk of relapse or progression as post-auto-HSCT consolidation,
- 3) Previously untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with chemotherapy, and
- 4) Systemic anaplastic large cell lymphoma (sALCL) after failure of at least one prior multi-agent chemotherapy regimen.

CLASSICAL HODGKIN LYMPHOMA

Previously Untreated Stage III or IV Classical Hodgkin Lymphoma (HL)

Drug and Biologic Coverage Criteria

The ECHELON-1 open-label, multicenter international pivotal randomized phase 3 trial, randomized a total of 1334 patients, from November 2012 through January 2016; 670 treatment-naïve participants with stage III or IV Hodgkin's to standard therapy and assigned 664 others to brentuximab vedotin, doxorubicin, vinblastine, and dacarbazine (A+AVD).

Patients with previously untreated stage III or IV classic Hodgkin's lymphoma in patients were assigned to receive brentuximab vedotin, doxorubicin, vinblastine, and dacarbazine (A+AVD) (n =664) and standard-of-care ABVD (n = 670) doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) Efficacy was established based on modified progression-free survival (mPFS), defined as progression, death, or receipt of additional anticancer therapy for patients who are not in a complete response after completion of frontline therapy.

The primary outcome was the rate of modified progression-free survival at 2 years, defined as a composite risk of progression, death, or noncomplete response and the use of a different anticancer therapy.

All secondary efficacy endpoints, including development of neutropenia and peripheral neuropathy, also favored A+AVD.

At median follow-up of 2.9 years, this measurement reached 82.1% in the A+AVD group and 77.2% in the ABVD group.

Brentuximab vedotin, doxorubicin, vinblastine, and dacarbazine (A+AVD) compared with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) significantly improved the 2-year progression-free survival rate in the randomized ECHELON-1 trial in patients with previously untreated stage III or IV classic Hodgkin's lymphoma

The results of this Phase III study demonstrate the superior efficacy of A+AVD compared with ABVD as the first-line treatment for patients with advanced Hodgkin's lymphoma. [NCT01712490]

Classical Hodgkin Lymphoma Post-Autologous Hematopoietic Stem-Cell Transplantation (Auto-HSCT) Consolidation

A randomized, double-blind, placebo-controlled, phase 3 trial was conducted at 78 sites across North America and Europe in patients with unfavorable-risk relapsed or primary refractory classic HL who had undergone auto-HSCT (Moskowitz et al.)

Patients were randomly assigned, by fixed-block randomization with a computer-generated random number sequence, to receive 16 cycles of 1.8 mg/kg brentuximab vedotin or placebo intravenously every 3 weeks, starting 30–45 days after transplantation.

Randomization was stratified by best clinical response after completion of salvage chemotherapy (complete response vs partial response vs stable disease) and primary refractory HL versus relapsed disease less than 12 months after completion of frontline therapy versus relapse 12 months or more after treatment completion.

Patients and study investigators were masked to treatment assignment. The primary endpoint was progression-free survival by independent review, defined as the time from randomization to the first documentation of tumor progression or death. Analysis was by intention to treat.

Between April 6, 2010, and Sept 21, 2012, 329 patients were randomly assigned to the brentuximab vedotin group (n=165) or the placebo group (n=164). Progression-free survival by independent review was significantly improved in patients in the brentuximab vedotin group compared with those in the placebo group (hazard ratio [HR] 0.57, 95% CI 0.40–0.81; p=0.0013). Median progression-free survival by independent review was 42.9 months (95% CI 30.4–42.9) for patients in the brentuximab vedotin group compared with 24.1 months (11.5–not estimable) for those in the placebo group. There was consistent benefit (HR <1) of brentuximab vedotin consolidation recorded across subgroups. The most frequent adverse events in the brentuximab vedotin group were peripheral sensory neuropathy (94 [56%] of 167 patient's vs 25 [16%] of 160 patients in the placebo group) and

Drug and Biologic Coverage Criteria

neutropenia (58 [35%] vs 19 [12%] patients). At time of analysis, 28 (17%) of 167 patients had died in the brentuximab vedotin group compared with 25 (16%) of 160 patients in the placebo group.

Early consolidation with brentuximab vedotin after autologous stem-cell transplantation improved progression-free survival in patients with HL with risk factors for relapse or progression after transplantation. This treatment provides an important therapeutic option for patients undergoing autologous stem-cell transplantation. [NCT01100502]

Classical Hodgkin Lymphoma, Relapsed

A multinational, open-label, phase II study the efficacy and safety of brentuximab vedotin were evaluated in 102 patients with relapsed or refractory Hodgkin lymphoma after autologous stem cell transplant. (Younes A, et al.)

Patients had histologically documented CD30-positive Hodgkin lymphoma by central pathology review. Brentuximab vedotin was administered 1.8 mg/kg every 3 weeks as a 30-minute outpatient IV infusion for up to 16 cycles. Median age was 31 years (age range, 15 to 77 years) and 53% of patients were women.

The median number of prior cancer-related systemic therapies was 3.5 (range, 1 to 13); 71% had primary refractory disease and 42% had not responded to their most recent prior therapy. The median number of cycles received was 9 (range, 1 to 16), with a median duration of treatment of 27 weeks (range, 3 to 54).

An objective response (greater than 50% tumor shrinkage) was achieved in 75% (76/102) of patients, and 34% (35 patients) achieved complete remission. Tumor size was reduced in 95% (97 patients). Symptoms resolved in 83% (29/35) of patients with symptoms at baseline. Among patients achieving complete remission, the median duration of response was not reached at the time initial results were reported, with a median follow-up of 1 year.

Overall progression-free survival (PFS) was 25 weeks by independent review and 39 weeks by investigator assessment; however, at the time initial results were reported, PFS was not reached in patients who achieved complete remission. [NCT00848926]

The most common treatment-related adverse events were peripheral sensory neuropathy, nausea, fatigue, neutropenia, and diarrhea. The ADC brentuximab vedotin was associated with manageable toxicity and induced objective responses in 75% of patients with relapsed or refractory HL after auto-SCT. Durable CRs approaching 2 years were observed, supporting study in earlier lines of therapy.

Systemic Anaplastic Large-Cell Lymphoma (sALCL), Relapsed

A Phase 2 Study of SGN-35 in Treatment of Patients with Relapsed or Refractory Systemic Anaplastic Large Cell Lymphoma (sALCL)

This is a single-arm, open-label, multicenter, clinical trial to evaluate the efficacy and safety of brentuximab vedotin (SGN-35) as a single agent in patients with relapsed or refractory ALCL. Patients with systemic ALCL and recurrent disease after at least one prior therapy received brentuximab vedotin 1.8 mg/kg intravenously every 3 weeks over 30 minutes as an outpatient infusion.

The primary end point of the study was overall objective response rate as assessed by independent central review.

Of 58 patients treated in the study, 50 patients (86%) achieved an objective response, 33 patients (57%) achieved a complete remission (CR), and 17 patients (29%) achieved a partial remission.

The median durations of overall response and CR were 12.6 and 13.2 months, respectively. Grade 3 or 4 adverse events in $\geq 10\%$ of patients were neutropenia (21%), thrombocytopenia (14%), and peripheral sensory neuropathy (12%). Brentuximab vedotin induced objective responses in the majority of patients and CRs in more than half of patients with sALCL. Approval is based on overall response rates of 86%, with a median duration of response of 12.6 months [NCT00866047].

Primary Cutaneous Anaplastic Large-Cell Lymphoma and CD30-expressing Mycosis

Fungoides

A Phase 3 Trial of Brentuximab Vedotin versus Physician's Choice (Methotrexate or Bexarotene) in CD30-Positive Cutaneous T-Cell Lymphoma (ALCANZA)

An international, open-label, randomized, phase 3, multicenter trial in adult patients with CD30- positive mycosis fungoides or primary cutaneous anaplastic large-cell lymphoma who had been previously treated (Prince et al.) was conducted across 52 centers in 13 countries.

Patients were randomly assigned (1:1) to receive intravenous brentuximab vedotin 1.8 mg/kg once every 3 weeks, for up to 16 3-week cycles, or physician's choice (oral methotrexate 5- 50mg once per week or oral bexarotene 300 mg/m² once per day) for up to 48 weeks.

The primary endpoint was the proportion of patients in the intention-to-treat population achieving an objective global response lasting at least 4 months per independent review facility. Safety analyses were done in all patients who received at least one dose of study drug. Between Aug 13, 2012, and July 31, 2015, 131 patients were enrolled and randomly assigned to a group (66 to brentuximab vedotin and 65 to physician's choice), with 128 analyzed in the intention-to-treat population (64 in each group).

At a median follow-up of 22.9 months (95% CI 18.4-26.1), the proportion of patients achieving an objective global response lasting at least 4 months was 56.3% (36 of 64 patients) with brentuximab vedotin versus 12.5% (eight of 64) with physician's choice, resulting in a between- group difference of 43.8% (95% CI 29.1-58.4; p<0.0001).

Grade 3-4 adverse events were reported in 27 (41%) of 66 patients in the brentuximab vedotin group and 29 (47%) of 62 patients in the physician's choice group. Peripheral neuropathy was seen in 44 (67%) of 66 patients in the brentuximab vedotin group (n=21 grade 2, n=6 grade 3) and four (6%) of 62 patients in the physician's choice group. One of the four on-treatment deaths was deemed by the investigator to be treatment-related in the brentuximab vedotin group; no on- treatment deaths were reported in the physician's choice group. Significant improvement in objective response lasting at least 4 months was seen with brentuximab vedotin versus physician's choice of methotrexate or bexarotene. [NCT01578499]

Lymphomatoid papulosis (LyP) is a recurrent, self-healing papulonodular skin eruption that is part of the group of cutaneous CD30+ lymphoproliferative disorders that includes primary cutaneous anaplastic large cell lymphoma (pcALCL) and borderline CD30+ lesions.

Systemic Anaplastic Large Cell Lymphoma and Other CD30-Expressing Peripheral T-Cell Lymphomas

Randomized Clinical Trial in Previously Untreated Systemic Anaplastic Large Cell Lymphoma or Other CD30-Expressing Peripheral T-Cell Lymphomas (ECHELON-2, NCT01777152)

The efficacy of ADCETRIS in combination with chemotherapy for the treatment of adult patients with previously untreated, CD30-expressing PTCL was evaluated in a multicenter, randomized, double-blind, double-dummy, actively controlled trial. For enrollment, the trial required CD30 expression ≥10% per immunohistochemistry. The trial excluded patients with primary cutaneous CD30-positive T-cell lymphoproliferative disorders and lymphomas. Of the 452 total patients, 226 patients were randomized to the ADCETRIS + CHP arm and 226 patients were randomized to the CHOP arm. Patients in both treatment arms were treated intravenously on Day 1 of each 21-day cycle for 6 to 8 cycles; prednisone was administered orally on Days 1-5. The median age was 58 years (range: 18 to 85), 63% were male, 62% were White, 22% were Asian, and 78% had an ECOG performance status of 0-1. Of the 452 patients enrolled, the disease subtypes included patients with systemic ALCL [70%; 48% anaplastic lymphoma kinase (ALK) negative and 22% ALK positive], PTCL not otherwise specified (16%), angioimmunoblastic T-cell lymphoma (12%), adult T-cell leukemia/lymphoma (2%), and enteropathy-associated T-cell lymphoma (<1%). Most patients had Stage III or IV disease (81%) and a baseline international prognostic index of 2 or 3 (63%). During randomized treatment, on the ADCETRIS + CHP arm, 70% of patients received 6 cycles and 18% of patients received 8 cycles. On the CHOP arm, 62% of patients received 6 cycles and 19% received 8 cycles.

Drug and Biologic Coverage Criteria

Efficacy was based on IRF-assessed PFS, which was defined as time from randomization to progression, death due to any cause, or receipt of subsequent anticancer chemotherapy to treat residual or progressive disease. Other efficacy endpoints included PFS in patients with systemic ALCL, overall survival, complete response rate, and overall response rate. Median overall survival was not reached in either treatment arm.

Breast implant-associated anaplastic large cell lymphoma is an uncommon peripheral T cell lymphoma (PTCL) arising around textured-surface breast implants placed for either reconstructive or cosmetic indications.

Adult T-cell leukemia/lymphoma (ATLL) is another CD30+ mature T-cell lymphoma under the larger histological classification of PTCL. Support for use in initial ATLL treatment in combination with CHP (cyclophosphamide, doxorubicin, and prednisone) comes from the ECHELON-2 double-blind, double-dummy, randomised, placebo-controlled, active-comparator phase 3 study. This found that front-line treatment with A+CHP is superior to CHOP for patients with CD30-positive peripheral T-cell lymphomas as shown by a significant improvement in progression-free survival and overall survival with a manageable safety profile. Support for use in relapsed/refractory ATLL is based on a subset analysis of PTCL from a phase 2 trial in relapsed/refractory CD30+ non-Hodgkin lymphoma (Horwitz et al., 2014). This same study (NCT01421667) also produced a subset analysis of patients with CD30+ B-cell lymphomas, including DLBCL and other B-cell lymphomas. Overall, significant activity with brentuximab vedotin was observed in relapsed/refractory DLBCL, and responses occurred across a range of CD30 expression (Jacobsen et al., 2015).

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Adcetris (brentuximab vedotin) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Adcetris (brentuximab vedotin) include: concomitant use with bleomycin due to pulmonary toxicity, patients with severe renal impairment (CrCl < 30 mL/min), patients with moderate or severe hepatic impairment (Child-Pugh B or C), pregnancy.

OTHER SPECIAL CONSIDERATIONS:

Adcetris (brentuximab vedotin) has a black box warning for progressive multifocal leukoencephalopathy (PML).

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J9042	injection, brentuximab vedotin, 1mg

AVAILABLE DOSAGE FORMS:

Adcetris SOLR 50MG (Single dose vial)

REFERENCES

1. Adcetris (brentuximab vedotin) [prescribing information]. Bothell, WA: Seagen Inc; November 2022.
2. Connors JM, Jurczak W., Straus, DJ., et al. Brentuximab Vedotin with Chemotherapy for Stage III or IV Hodgkin's Lymphoma. Echelon-1 ClinicalTrials.gov number, NCT01712490 N Engl J Med. 2018; 378:331-344. PMID: 29224502
3. Moskowitz CH, Nademanee A, Masszi T, et al. Brentuximab vedotin as consolidation therapy after

Drug and Biologic Coverage Criteria

autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): a randomized, double-blind, placebo-controlled, phase 3 trial. ClinicalTrials.gov, number NCT01100502. Lancet. 2015 May 9; 385(9980):1853-62. PMID: 25796459

4. Pro B, Advani R, Brice P, et al. Brentuximab vedotin (SGN-35) in patients with relapsed or refractory systemic anaplastic large-cell lymphoma: results of a phase II study. J Clin Oncol. 2012 Jun 20; 30 (18). PMID: 22614995. Available at: <http://ascopubs.org/doi/full/10.1200/JCO.2011.38.0402> Accessed October 2018
5. Prince HM, Kim YH, Horwitz SM, et al. Brentuximab vedotin or physician's choice in CD30- positive cutaneous T-cell lymphoma (ALCANZA): an international, open-label, randomized, phase 3, multicenter trial. Lancet. 2017 Aug 5; 390(10094):555-566. PMID: 28600132
6. Younes A, Gopal AK, Smith SE, et al. Results of a Pivotal Phase II Study of Brentuximab Vedotin for Patients With Relapsed or Refractory Hodgkin's Lymphoma. Journal of Clinical Oncology. 2012;30(18):2183-2189. doi:10.1200/JCO.2011.38.0410.
7. Kim, YH, Tavallaee, M, Sundram, U, et al. Phase II Investigator-Initiated Study of Brentuximab Vedotin in Mycosis Fungoides and Sezary Syndrome With Variable CD30 Expression Level: A Multi-Institution Collaborative Project. J Clin Oncol. 2015 Nov 10;33(32):3750-8. PMID: 26195720
8. Duvic, M, Tetzlaff, MT, Gangar, P, Clos, AL, Sui, D, Talpur, R. Results of a Phase II Trial of Brentuximab Vedotin for CD30+ Cutaneous T-Cell Lymphoma and Lymphomatoid Papulosis. J Clin Oncol. 2015 Nov 10;33(32):3759-65. PMID: 26261247
9. Horwitz, SM, Advani, RH, Bartlett, NL, et al. Objective responses in relapsed T-cell lymphomas with single-agent brentuximab vedotin. Blood. 2014 May 15;123(20):3095- 100.PMID: 24652992
10. NCCN Clinical Practice Guidelines in Oncology™. T-cell Lymphomas v.2.2019 [Updated December 17, 2018]. [cited 12/30/2020]; Available from: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf
11. NCCN Clinical Practice Guidelines in Oncology™. Hodgkin Lymphoma v.2.2019 [Updated July 15, 2019]. [cited 12/30/2020]; Available from: https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf
12. National Cancer Institute. Surveillance, Epidemiology, and End Results (SEER) Program. Cancer Stat Facts: Hodgkin Lymphoma. Available at: <https://seer.cancer.gov/statfacts/html/hodg.html>
13. National Comprehensive Cancer Network. 2022. Hodgkin Lymphoma (Version 2.2023). [online] Available at: <[hodgkins.pdf \(nccn.org\)](#)> [Accessed 28 December 2022].
14. National Comprehensive Cancer Network. 2022. T-Cell Lymphomas (Version 2.2022). [online] Available at: <[t-cell.pdf \(nccn.org\)](#)> [Accessed 28 December 2022].
15. National Comprehensive Cancer Network. 2022. B-Cell Lymphomas (Version 5.2022). [online] Available at: <[b-cell.pdf \(nccn.org\)](#)> [Accessed 28 December 2022].
16. National Comprehensive Cancer Network. 2022. Primary Cutaneous Lymphoma (Version 2.2022). [online] Available at: <[primary_cutaneous.pdf \(nccn.org\)](#)> [Accessed 28 December 2022].
17. Moskowitz, C. H., Walewski, J., Nademanee, A., Masszi, T., Agura, E., Holowiecki, J., Abidi, M. H., Chen, A. I., Stiff, P., Viviani, S., Bachanova, V., Sureda, A., McClendon, T., Lee, C., Lisano, J., & Sweetenham, J. (2018). Five-year PFS from the AETHERA trial of brentuximab vedotin for Hodgkin lymphoma at high risk of progression or relapse. Blood, 132(25), 2639–2642. <https://doi.org/10.1182/blood-2018-07-861641>
18. Horwitz, S. M., Advani, R. H., Bartlett, N. L., Jacobsen, E. D., Sharman, J. P., O'Connor, O. A., . . . Oki, Y. (2014). Objective responses in relapsed T-cell lymphomas with single-agent Brentuximab Vedotin. Blood, 123(20), 3095-3100. doi:10.1182/blood-2013-12-542142
19. Horwitz, S., O'Connor, O. A., Pro, B., Illidge, T., Fanale, M., Advani, R., . . . Zinzani, P. L. (2019). Brentuximab Vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma (echelon-2): A global, double-blind, randomised, phase 3 trial. The Lancet, 393(10168), 229-240. doi:10.1016/s0140-6736(18)32984-2
20. Jacobsen, E. D., Sharman, J. P., Oki, Y., Advani, R. H., Winter, J. N., Bello, C. M., . . . Bartlett, N. L. (2015). Brentuximab vedotin demonstrates objective responses in a phase 2 study of relapsed/refractory DLBCL with variable CD30 expression. Blood, 125(9), 1394-1402. doi:10.1182/blood-2014-09-598763

Molina Healthcare, Inc. confidential and proprietary © 2023

This document contains confidential and proprietary information of Molina Healthcare and cannot be reproduced, distributed, or printed without written permission from Molina Healthcare. This page contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with Molina Healthcare.

Drug and Biologic Coverage Criteria

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Age Restrictions Quantity FDA-Approved Uses Background Contraindications/Exclusions/Discontinuation Other Special Considerations References	Q1 2023
Q2 2022 Established tracking in new format	Historical changes on file