Adcetris® (brentuximab vedotin)
(Intravenous)

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I. Length of Authorization [1,7,18]

Coverage will be provided for six months and may be renewed.

- Treatment for Adult cHL post-auto HSCT, Pediatric cHL, Mycosis Fungoides (MF)/Sezary Syndrome (SS), and Primary Cutaneous CD30+ T-Cell Lymphoproliferative Disorders has a maximum of 16 cycles.
- Treatment of previously untreated Adult Stage III or IV Classical Hodgkin Lymphoma (cHL) has a maximum of 12 doses.
- Treatment of previously untreated Systemic Anaplastic Large Cell Lymphoma (sALCL) or other CD30-expressing Peripheral T-Cell Lymphomas (PTCL) has a maximum of 8 doses.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- 50 mg vial: 4 vials per 21 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 200 billable units per 21 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age (unless otherwise specified); **AND**

Universal Criteria [1]

- Patient has CD30-positive disease; **AND**
- Patient must not be receiving concomitant bleomycin; **AND**
- Patient does not have severe renal impairment (i.e., CrCl <30 mL/min); **AND**
- Patient does not have moderate or severe hepatic impairment (Child-Pugh B or C); **AND**

Adult Classic Hodgkin Lymphoma (cHL) † [1,2,4,12-14]

- Used as single agent therapy; **AND**
  - Used as consolidation/maintenance therapy post-autologous hematopoietic stem cell transplant (auto-HSCT) in patients at high risk* for relapse or progression † ‡; **OR**
  - Patient has relapsed disease after failure of auto-HSCT or after failure of at least 2 prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates †; **OR**
  - Used as subsequent systemic therapy (if not previously used) for relapsed or refractory disease ‡; **OR**
  - Used as palliative therapy for relapsed or refractory disease in patients >60 years of age ‡; **OR**
- Used in combination with bendamustine; **AND**
  - Used as subsequent systemic therapy (if not previously used) for relapsed or refractory disease ‡; **OR**
- Used in combination with nivolumab; **AND**
  - Used as subsequent systemic therapy (if not previously used) for relapsed or refractory disease ‡; **OR**
- Used in combination with dacarbazine; **AND**
  - Used as primary treatment in patients >60 years of age with stage I-II unfavorable or stage III-IV disease ‡; **OR**
- Used in combination with doxorubicin, vinblastine, and dacarbazine (AVD); **AND**
  - Used as initial therapy for previously untreated stage III or IV disease †; **OR**
  - Used as initial therapy for previously untreated stage II unfavorable disease in patients >60 years of age ‡

**High risk for relapse or progression may be defined as:*
- *Refractory disease, relapse within 12 months, or extranodal disease following frontline therapy OR 2 or more of the following: PET+ response at time of transplant, B symptoms, and/or >1 salvage/subsequent therapy regimen)*

Pediatric Classic Hodgkin Lymphoma (cHL) ‡ Φ [2]

- Patient is ≤18 years of age; **AND**
- Patient has relapsed or refractory disease; **AND**
  - Used as re-induction or subsequent therapy; **AND**
    - Used in combination with nivolumab or gemcitabine; **AND**
      - Used in heavily pretreated patients with platinum or anthracycline-based chemotherapy; **OR**
      - Used if a decrease in cardiac function is observed

T-Cell Lymphomas [1-3,15,16]

- Peripheral T-Cell Lymphoma (PTCL)
  - Used as a single agent after failure of at least one prior chemotherapy regimen for one of the following:

- Systemic Anaplastic Large Cell Lymphoma (sALCL) † Φ
- Peripheral T-Cell Lymphoma (PTCL) ‡ Φ
- Angioimmunoblastic T-cell Lymphoma (AITL) ‡ Φ; **OR**

  - Used in combination with cyclophosphamide, doxorubicin, and prednisone (CHP) in patients with CD30 expression ≥ 10% per immunohistochemistry (IHC) as initial therapy for previously untreated:
    - Systemic Anaplastic Large Cell Lymphoma (sALCL) † Φ
    - Peripheral T-Cell Lymphoma (PTCL) not otherwise specified † Φ
    - Angioimmunoblastic T-cell Lymphoma (AITL) † Φ

Primary Cutaneous Lymphomas [1,2,17]

- Mycosis Fungoides (MF) † Φ/Sezary Syndrome (SS) ‡ Φ
  - Used as a single agent; **AND**
    - Used as subsequent therapy *(excluding patients with relapsed or persistent stage IA-IIA MF with B1 blood involvement)*; **AND**
    - Patient has CD30 expression ≥ 5% per IHC
- Primary Cutaneous CD30+ T-Cell Lymphoproliferative Disorders ‡ Φ
  - Used as a single agent in patients previously treated with systemic therapy; **AND**
    - Patient has primary cutaneous anaplastic large cell lymphoma (pcALCL) †; **OR**
    - Patient has cutaneous ALCL with regional node (N1) *(excludes systemic ALCL)*; **OR**
    - Patient has lymphomatoid papulosis (LyP) with extensive lesions that is relapsed or refractory to all treatment options (e.g., clinical trial, observation, retreatment with primary treatment, or treatment with alternative regimen)

B-Cell Lymphomas ‡ [2,11]

- Diffuse Large B-Cell Lymphoma (DLBCL)
  - Used as subsequent therapy for partial response, no response, relapsed, progressive, or refractory DLBCL in non-candidates for transplant
- Histologic transformation of Follicular Lymphoma or Nodal Marginal Zone Lymphoma to Diffuse Large B-Cell Lymphoma (DLBCL)
  - Patient has received multiple lines of chemoimmunotherapy (e.g., BR, RCHOP, etc.) for transformed or indolent disease

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA Approved Indication(s), ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based on the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: progressive multifocal leukoencephalopathy, peripheral neuropathy, anaphylaxis and infusion reactions, hematologic toxicities (thrombocytopenia, neutropenia and anemia), serious infections, opportunistic infections, tumor lysis syndrome, hepatotoxicity, pulmonary toxicity, serious dermatologic reactions, gastrointestinal complications, uncontrolled hyperglycemia, etc.

V. Dosage/Administration [1,7]

Indication	Dose
Previously Untreated Stage III or IV Adult Classical Hodgkin Lymphoma	1.2 mg/kg (up to 120 mg) by intravenous infusion every 2 weeks until a maximum of 12 doses, disease progression, or unacceptable toxicity
Adult cHL post-auto HSCT, MF/SS, Primary Cutaneous CD30+ T-Cell Lymphoproliferative Disorders	1.8 mg/kg (up to 180 mg) by intravenous infusion every 3 weeks until a maximum of 16 cycles, disease progression, or unacceptable toxicity
Pediatric cHL	1.8 mg/kg (up to 180 mg) by intravenous infusion every 3 weeks until a maximum of 16 cycles, disease progression, or unacceptable toxicity
Previously Untreated sALCL or Other CD30-expressing PTCL	1.8 mg/kg (up to 180 mg) by intravenous infusion every 3 weeks with each cycle of chemotherapy for a maximum of 6 to 8 doses
All other indications	1.8 mg/kg (up to 180 mg) by intravenous infusion every 3 weeks until disease progression or unacceptable toxicity

VI. Billing Code/Availability Information

HCPCS Code:

- J9042 - Injection, brentuximab vedotin, 1 mg; 1 billable unit = 1 mg

NDC:

- Adcetris single-use vial; 50 mg powder for injection: 51144-0050-xx

VII. References (STANDARD)

1. Adcetris [package insert]. Bothell, WA; Seattle Genetics, Inc; October 2019. Accessed February 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for brentuximab vedotin. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2021.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) T-Cell Lymphomas. Version 1.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2021.
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Hodgkin Lymphoma, Version 2.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2021.
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12. Connors JM, Jurczak W, Straus DJ, et al. Brentuximab Vedotin with Chemotherapy for Stage III or IV Hodgkin's Lymphoma [published correction appears in N Engl J Med. 2018 Mar 1;378(9):878]. N Engl J Med. 2018;378(4):331-344.
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VIII. References (ENHANCED)

1e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Primary Cutaneous Lymphomas, Version 1.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2021.

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C81.10	Nodular sclerosis Hodgkin lymphoma, unspecified site
C81.11	Nodular sclerosis Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.12	Nodular sclerosis Hodgkin lymphoma, intrathoracic lymph nodes
C81.13	Nodular sclerosis Hodgkin lymphoma, intra-abdominal lymph nodes
C81.14	Nodular sclerosis Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.15	Nodular sclerosis Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.16	Nodular sclerosis Hodgkin lymphoma, intrapelvic lymph nodes
C81.17	Nodular sclerosis Hodgkin lymphoma, spleen
C81.18	Nodular sclerosis Hodgkin lymphoma, lymph nodes of multiple sites
C81.19	Nodular sclerosis Hodgkin lymphoma, extranodal and solid organ sites
C81.20	Mixed cellularity Hodgkin lymphoma, unspecified site
C81.21	Mixed cellularity Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.22	Mixed cellularity Hodgkin lymphoma, intrathoracic lymph nodes
C81.23	Mixed cellularity Hodgkin lymphoma, intra-abdominal lymph nodes
C81.24	Mixed cellularity Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.25	Mixed cellularity Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.26	Mixed cellularity Hodgkin lymphoma, intrapelvic lymph nodes
C81.27	Mixed cellularity Hodgkin lymphoma, spleen

ICD-10	ICD-10 Description
C81.28	Mixed cellularity Hodgkin lymphoma, lymph nodes of multiple sites
C81.29	Mixed cellularity Hodgkin lymphoma, extranodal and solid organ sites
C81.30	Lymphocyte depleted Hodgkin lymphoma, unspecified site
C81.31	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.32	Lymphocyte depleted Hodgkin lymphoma, intrathoracic lymph nodes
C81.33	Lymphocyte depleted Hodgkin lymphoma, intra-abdominal lymph nodes
C81.34	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.35	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.36	Lymphocyte depleted Hodgkin lymphoma, intrapelvic lymph nodes
C81.37	Lymphocyte depleted Hodgkin lymphoma, spleen
C81.38	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of multiple sites
C81.39	Lymphocyte depleted Hodgkin lymphoma, extranodal and solid organ sites
C81.40	Lymphocyte-rich Hodgkin lymphoma, unspecified site
C81.41	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.42	Lymphocyte-rich Hodgkin lymphoma, intrathoracic lymph nodes
C81.43	Lymphocyte-rich Hodgkin lymphoma, intra-abdominal lymph nodes
C81.44	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.45	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.46	Lymphocyte-rich Hodgkin lymphoma, intrapelvic lymph nodes
C81.47	Lymphocyte-rich Hodgkin lymphoma, spleen
C81.48	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of multiple sites
C81.49	Lymphocyte-rich Hodgkin lymphoma, extranodal and solid organ sites
C81.70	Other Hodgkin lymphoma unspecified site
C81.71	Other Hodgkin lymphoma lymph nodes of head, face, and neck
C81.72	Other Hodgkin lymphoma intrathoracic lymph nodes
C81.73	Other Hodgkin lymphoma intra-abdominal lymph nodes
C81.74	Other Hodgkin lymphoma lymph nodes of axilla and upper limb
C81.75	Other Hodgkin lymphoma lymph nodes of inguinal region and lower limb
C81.76	Other Hodgkin lymphoma intrapelvic lymph nodes
C81.77	Other Hodgkin lymphoma spleen
C81.78	Other Hodgkin lymphoma lymph nodes of multiple sites
C81.79	Other Hodgkin lymphoma extranodal and solid organ sites
C81.90	Hodgkin lymphoma, unspecified, unspecified site
C81.91	Hodgkin lymphoma, unspecified, lymph nodes of head, face and neck

ICD-10	ICD-10 Description
C81.92	Hodgkin lymphoma, unspecified, intrathoracic lymph nodes
C81.93	Hodgkin lymphoma, unspecified, intra-abdominal lymph nodes
C81.94	Hodgkin lymphoma, unspecified, lymph nodes of axilla and upper limb
C81.95	Hodgkin lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C81.96	Hodgkin lymphoma, unspecified, intrapelvic lymph nodes
C81.97	Hodgkin lymphoma, unspecified, spleen
C81.98	Hodgkin lymphoma, unspecified, lymph nodes of multiple sites
C81.99	Hodgkin lymphoma, unspecified, extranodal and solid organ sites
C83.30	Diffuse large B-cell lymphoma unspecified site
C83.31	Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
C83.32	Diffuse large B-cell lymphoma intrathoracic lymph nodes
C83.33	Diffuse large B-cell lymphoma intra-abdominal lymph nodes
C83.34	Diffuse large B-cell lymphoma lymph nodes of axilla and upper limb
C83.35	Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.36	Diffuse large B-cell lymphoma intrapelvic lymph nodes
C83.37	Diffuse large B-cell lymphoma, spleen
C83.38	Diffuse large B-cell lymphoma lymph nodes of multiple sites
C83.39	Diffuse large B-cell lymphoma extranodal and solid organ sites
C84.00	Mycosis fungoides, unspecified site
C84.01	Mycosis fungoides, lymph nodes of head, face and neck
C84.02	Mycosis fungoides, intrathoracic lymph nodes
C84.03	Mycosis fungoides, intra-abdominal lymph nodes
C84.04	Mycosis fungoides, lymph nodes of axilla and upper limb
C84.05	Mycosis fungoides, lymph nodes of inguinal region and lower limb
C84.06	Mycosis fungoides, intrapelvic lymph nodes
C84.07	Mycosis fungoides, spleen
C84.08	Mycosis fungoides, lymph nodes of multiple sites
C84.09	Mycosis fungoides, extranodal and solid organ sites
C84.10	Sézary disease, unspecified site
C84.11	Sézary disease, lymph nodes of head, face, and neck
C84.12	Sézary disease, intrathoracic lymph nodes
C84.13	Sézary disease, intra-abdominal lymph nodes
C84.14	Sézary disease, lymph nodes of axilla and upper limb
C84.15	Sézary disease, lymph nodes of inguinal region and lower limb

ICD-10	ICD-10 Description
C84.16	Sézary disease, intrapelvic lymph nodes
C84.17	Sézary disease, spleen
C84.18	Sézary disease, lymph nodes of multiple sites
C84.19	Sézary disease, extranodal and solid organ sites
C84.40	Peripheral T-cell lymphoma, not classified, unspecified site
C84.41	Peripheral T-cell lymphoma, not classified, lymph nodes of head, face and neck
C84.42	Peripheral T-cell lymphoma, not classified, intrathoracic lymph nodes
C84.43	Peripheral T-cell lymphoma, not classified, intra-abdominal lymph nodes
C84.44	Peripheral T-cell lymphoma, not classified, lymph nodes of axilla and upper limb
C84.45	Peripheral T-cell lymphoma, not classified, lymph n odes of inguinal region of lower limb
C84.46	Peripheral T-cell lymphoma, not classified, intrapelvic lymph nodes
C84.47	Peripheral T-cell lymphoma, not classified, spleen
C84.48	Peripheral T-cell lymphoma, not classified, lymph nodes of multiple sites
C84.49	Peripheral T-cell lymphoma, not classified, extranodal and solid organ sites
C84.60	Anaplastic large cell lymphoma, ALK-positive, unspecified site
C84.61	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of head, face and neck
C84.62	Anaplastic large cell lymphoma, ALK-positive, intrathoracic lymph nodes
C84.63	Anaplastic large cell lymphoma, ALK-positive, intra-abdominal lymph nodes
C84.64	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of axilla and upper limb
C84.65	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of inguinal region and lower limb
C84.66	Anaplastic large cell lymphoma, ALK-positive, intrapelvic lymph nodes
C84.67	Anaplastic large cell lymphoma, ALK-positive, spleen
C84.68	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of multiple sites
C84.69	Anaplastic large cell lymphoma, ALK-positive, extranodal and solid organ sites
C84.70	Anaplastic large cell lymphoma, ALK-negative, unspecified site
C84.71	Anaplastic large cell lymphoma, ALK-negative, lymph nodes of head, face and neck
C84.72	Anaplastic large cell lymphoma, ALK-negative, intrathoracic lymph nodes
C84.73	Anaplastic large cell lymphoma, ALK-negative, intra-abdominal lymph nodes
C84.73	Anaplastic large cell lymphoma, ALK-negative, lymph nodes of axilla and upper limb
C84.75	Anaplastic large cell lymphoma, ALK-negative, lymph nodes of inguinal region and lower limb
C84.76	Anaplastic large cell lymphoma, ALK-negative, intrapelvic lymph nodes
C84.77	Anaplastic large cell lymphoma, ALK-negative, spleen
C84.78	Anaplastic large cell lymphoma, ALK-negative, lymph nodes of multiple sites
C84.79	Anaplastic large cell lymphoma, ALK-negative, extranodal and solid organ sites

ICD-10	ICD-10 Description
C85.20	Mediastinal (thymic) large B-cell lymphoma, unspecified site
C85.21	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face and neck
C85.22	Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes
C85.23	Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes
C85.24	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb
C85.25	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.26	Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes
C85.27	Mediastinal (thymic) large B-cell lymphoma, spleen
C85.28	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites
C85.29	Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites
C86.5	Angioimmunoblastic T-cell lymphoma
C86.6	Primary cutaneous CD30-positive T-cell proliferations
Z85.71	Personal history of Hodgkin lymphoma
Z85.72	Personal history of non-Hodgkin lymphomas

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Appendix 3 – CLINICAL LITERATURE REVIEW

OS = overall survival; PFS = progression-free survival; ORR = objective response rate; CR = complete response; PR = partial response; DoR = duration of response; TTP = time to progression; FFS = failure-free survival; EFS = event-free survival; PFR = progression free rate; pCR = pathological complete response; CMR = complete metabolic response

Adult Classic Hodgkin Lymphoma (cHL)

Consolidation/maintenance therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin	2A	Yes	Phase 3 (AETHERA), randomized, double-blind, placebo-controlled	Placebo	PFS	Relapsed or refractory disease at high risk of progression after ASCT	• Early consolidation with brentuximab vedotin after ASCT improved PFS in patients with Hodgkin's lymphoma with risk factors for relapse or progression after transplantation. There was no statistically significant difference in OS between the two groups.
Initial therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin (BV) + dacarbazine (DTIC)	2A (≥60y stage I-II unfavorable or stage III-IV disease)	No	Phase 2, randomized, open-label	Brentuximab vedotin + bendamustine vs. brentuximab	ORR	Initial therapy	• BV alone and BV+DTIC appear to induce long-term remissions for a subset of elderly HL pts. The addition of DTIC appears to increase durability of response and

			Long-term follow-up	vedotin monotherapy			survival although not statistically assessed.
Brentuximab + doxorubicin + vinblastine + dacarbazine (A+AVD)	2A (stage III-IV with no known neuropathy, IPS ≥4, or bleomycin contraindicated)	Yes (stage III-IV)	Phase 3 (ECHELON-1), randomized, open-label, multi-center	Doxorubicin + bleomycin + vinblastine + dacarbazine (ABVD)	PFS	Initial therapy	• A+AVD had superior efficacy to ABVD in the treatment of patients with advanced-stage Hodgkin's lymphoma, with a 4.9 percentage-point lower combined risk of progression, death, or noncomplete response and use of subsequent anticancer therapy at 2 years.
Brentuximab + doxorubicin + vinblastine + dacarbazine (A+AVD), followed by brentuximab	2A (stage III-IV disease or stage I-II unfavorable disease in patients > 60 years old)	Yes (stage III-IV)	Phase 2, multi-center	N/A	ORR	Initial therapy in patients > 60 years or older	• Sequential Brentuximab-AVD was well tolerated and was associated with an ORR of 95% in patients who received brentuximab initially followed by 6 cycles of AVD, followed by consolidative doses of brentuximab in responding patients.
Relapsed or refractory CD30-positive disease							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin	2A (second-line and later therapy)	Yes (after failure of HDT/ASCR or at least 2 prior chemo regimens in patients not	Phase 2 3-year follow-up	N/A	ORR	Relapsed or refractory CD30-positive disease after HDT/ASCR	• Brentuximab vedotin induced an ORR of 75% in patients with relapsed or refractory HL after auto-SCT.

		candidates for HDT/ASCR)					
Brentuximab vedotin (BV)	2A (second-line and later therapy)	Yes (after failure of HDT/ASCR or at least 2 prior chemo regimens in patients not candidates for HDT/ASCR)	Phase 2	N/A	ORR	First line salvage therapy in relapsed/refractory HL prior to ASCT	• BV as first line salvage therapy is efficacious, well tolerated, and does not hinder stem cell collection or engraftment. 90% of patients were effectively bridged to ASCT and 52% did not require multi-agent chemotherapy.
Bendamustine + brentuximab vedotin	2A (second-line or subsequent therapy)	No	Phase 1-2, multi-center	N/A	ORR	Relapsed or refractory disease after one previous line of chemo	• This study shows that brentuximab vedotin plus bendamustine, with a favorable safety profile, is an active salvage regimen for heavily pretreated patients with relapsed or refractory Hodgkin's lymphoma
Bendamustine + brentuximab vedotin	2A (second-line or subsequent therapy)	No	Phase 1-2	N/A	CR	Initial salvage therapy	• Brentuximab vedotin plus bendamustine as first salvage therapy in relapsed or refractory Hodgkin lymphoma demonstrated an ORR of 92.5% and CR rate of 73.6%.
Brentuximab vedotin + nivolumab (up to 4 cycles)	2A	No	Phase 1/2	N/A	CR	Initial salvage therapy	• The combination of brentuximab vedotin and nivolumab demonstrated an ORR of 82% as initial salvage therapy.

Pediatric Classic Hodgkin Lymphoma

Relapsed or refractory disease							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin + bendamustine	2A	No	Phase 1-2, multi-center	N/A	ORR	Relapsed or refractory disease after at least one previous line of chemo	• This study shows that brentuximab vedotin plus bendamustine, with a favorable safety profile, is an active salvage regimen for heavily pretreated adult patients with relapsed or refractory Hodgkin's lymphoma.
Brentuximab vedotin + gemcitabine	2A	No	Phase 2	N/A	CR	Refractory disease or relapse <1 year from initial treatment	• Brentuximab vedotin with gemcitabine demonstrated a CR rate of 67% in pediatric and young adult patients with primary refractory or early relapsed Hodgkin lymphoma.
Brentuximab vedotin + nivolumab	2A	No	Phase 2	N/A	CMR rate	Relapsed or refractory disease	• Primary analysis demonstrated a CMR rate of 88% and an ORR of 98% in children, adolescents, and young adults with relapsed or refractory classical Hodgkin lymphoma.

T-Cell Lymphomas

Systemic Anaplastic Large Cell Lymphoma (sALCL) – Initial therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin + cyclophosphamide + doxorubicin +	1 preferred	Yes	Phase 3 (ECHELON-2), double-blind, randomized	Cyclophosphamide + doxorubicin + vincristine + prednisone (CHOP)	PFS	Initial therapy	• 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

prednisone (A+CHP)							progression-free survival with a manageable safety profile.
Peripheral T-Cell Lymphoma (PTCL) – Initial therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin + cyclophosphamide + doxorubicin + prednisone (A+CHP)	2A preferred	Yes	Phase 3 (ECHELON-2), double-blind, randomized	Cyclophosphamide + doxorubicin + vincristine + prednisone (CHOP)	PFS	Initial therapy	• 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 with a manageable safety profile.
Systemic Anaplastic Large Cell Lymphoma (sALCL) – Relapsed or refractory disease							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin	1 (ALCL) 2A preferred for CD30+ PTCL	Yes (ALCL only)	Phase 2 (NCT00866047), multicenter, open-label, single-arm Long-term follow-up	N/A	ORR	After at least one prior therapy	• Brentuximab vedotin induced an ORR of 86% and CRs in more than half of patients with recurrent systemic ALCL
Peripheral T-Cell Lymphoma (PTCL) – Relapsed or refractory disease							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**

Brentuximab vedotin	1 (ALCL) 2A preferred for CD30+ PTCL	Yes (ALCL only)	Phase 2, open-label, multi-center	N/A	ORR	Relapsed or refractory disease	• Brentuximab vedotin showed antitumor activity in patients with relapsed PTCL particularly AITL with an overall ORR of 41% and ORR of 54% for AITL.
Breast-Implant Associated Anaplastic Large Cell Lymphoma							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin	2A	No	Case report	N/A	-----	Second line	• Adjuvant chemotherapy may be required for more invasive disease and our experience has shown the efficacy of Brentuximab as a second line treatment.
Brentuximab vedotin	2A	No	Case report	N/A	-----	Initial therapy	• This is the first report on the use of brentuximab vedotin in a frontline setting for treatment of BIA-ALCL.
Adult T-Cell Leukemia/Lymphoma							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin	2A	No	Phase 3 (ECHELON-2), double-blind, randomized	Cyclophosphamide + doxorubicin + vincristine + prednisone (CHOP)	PFS	Initial therapy	• 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 with a manageable safety profile.
Mogamulizumab	2A preferred (second-line	No	Phase 2, multicenter	N/A	ORR	After at least one prior therapy	• Mogamulizumab monotherapy may improve PFS and OS in some patients with relapsed aggressive ATL, especially those who develop a

	or subsequent therapy)		Follow-up analysis				skin rash as a moderate immune-related adverse event
Extranodal NK/T-Cell Lymphoma							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin	2A preferred	No	No clinical evidence to support indication.				
Pembrolizumab	2A	No	Study group analysis	N/A	-----	Relapsed or refractory disease after asparaginase regimen	• PD1 blockade with pembrolizumab was effective with an ORR of 100% for NK/T-cell lymphomas failing l-asparaginase regimens.
Hepatosplenic Gamma-Delta T-Cell Lymphoma							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin	2A	No	No clinical evidence to support indication.				
Mycosis Fungoides (MF) / Sezary Syndrome (SS)							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin	2A preferred (primary therapy and for relapsed or	Yes (CD30+ MF relapsed or refractory disease only)	Phase 3 (ALCANZA), international, open-label,	Physician's Choice (methotrexate or bexarotene)	ORR ≥ 4 months	After at least one prior systemic therapy	• Significant improvement in objective response lasting at least 4 months was seen with brentuximab vedotin versus physician's choice of methotrexate or bexarotene

	refractory disease)		randomized, multicenter				
Brentuximab vedotin	2A preferred (primary therapy and for relapsed or refractory disease)	Yes (CD30+ MF relapsed or refractory disease only)	Phase 2	N/A	ORR	After at least one prior systemic therapy with negligible to 100% CD30 expression	• Brentuximab vedotin demonstrated significant clinical activity with an ORR of 70% in treatment-refractory or advanced MF or SS with a wide range of CD30 expression levels.
Primary cutaneous CD30+ T-Cell Lymphoproliferative Disorders							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin	2A preferred (primary therapy and for relapsed or refractory disease)	Yes (CD30+ MF relapsed or refractory disease only)	Phase 3 (ALCANZA), international, open-label, randomized, multicenter	Physician's Choice (methotrexate or bexarotene)	ORR ≥ 4 months	After at least one prior systemic therapy	• Significant improvement in objective response lasting at least 4 months was seen with brentuximab vedotin versus physician's choice of methotrexate or bexarotene
Brentuximab vedotin	2A preferred (primary therapy and for relapsed or refractory disease)	Yes (CD30+ MF relapsed or refractory disease only)	Phase 2, open-label	N/A	------	After at least one prior systemic therapy (MF, pcALCL)	• Brentuximab vedotin is both active and well tolerated in cutaneous T-cell lymphoma with an ORR of 73% and CR of 35%.
Histologic transformation of follicular lymphoma or marginal zone lymphoma to Diffuse Large B-Cell Lymphoma							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**

Brentuximab vedotin	2A	No	Phase 2, open-label	None	ORR	Relapsed or refractory NHL	• Overall, activity with brentuximab vedotin was demonstrated with an ORR of 44% in relapsed/refractory DLBCL, and responses occurred across a range of CD30 expression.
Diffuse Large B-cell Lymphoma							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin	2A	No	Phase 2, open-label	None	ORR	Relapsed or refractory NHL	• Overall, activity with brentuximab vedotin was demonstrated with an ORR of 44% in relapsed/refractory DLBCL, and responses occurred across a range of CD30 expression.
Primary Cutaneous DLBCL							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin	2A	No	No clinical evidence to support use.				
High grade B-cell lymphoma							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin	2A	No	No clinical evidence to support use.				
AIDS-related DLBCL, primary effusion lymphoma, and HHV8-positive DLBCL							

Regimen	NCCN Category	FDA Approved	Trial Design	Comparator	Primary End-Point	Line of Therapy	Conclusion
Brentuximab vedotin	2A	No	Case report for primary effusion lymphoma	N/A	-----	Refractory to da-EPOCH	• One patient with AIDS-related primary effusion lymphoma achieved a complete response for over 39 months with brentuximab vedotin.
Brentuximab vedotin	2A	No	Case report HIV-associated lymphoma	N/A	-----	Relapsed disease	• This case report presents 2 patients with relapsed HIV-associated lymphoma who experienced a second complete remission after treatment with the immunotherapy agent brentuximab vedotin.
CD30+ monomorphic PTLD (B-cell type)							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Brentuximab vedotin	2A	No	No clinical evidence to support use.				