Drug Policy:

Adcetris™ (brentuximab vedotin)

POLICY NUMBER UM ONC_1203	SUBJECT Adcetris™ (brentuximab vedotin)		DEPT/PROGRAM UM Dept	PAGE 1 OF 5
DATES COMMITTEE REVIEWED 02/08/12, 10/13/13, 12/04/14, 07/26/16, 08/10/17, 08/08/18, 07/10/19, 10/09/19, 12/11/19, 04/08/20, 12/09/20, 02/10/21, 11/15/21, 01/12/22	APPROVAL DATE January 12, 2022	EFFECTIVE DATE January 28, 2022	COMMITTEE APPROVAL DATES 02/08/12, 10/13/13, 12/04/14, 07/26/16, 08/10/17, 08/08/18, 07/10/19, 10/09/19, 12/11/19, 04/08/20, 12/09/20, 02/10/21, 11/15/21, 01/12/22	
PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS HUM 1	NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT	
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Adcetris (brentuximab vedotin) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:

1. When health plan Medicaid coverage provisions—including any applicable PDLs (Preferred Drug Lists)—conflict with the coverage provisions in this drug policy, health plan Medicaid coverage provisions take precedence per the Preferred Drug Guidelines OR
2. When health plan Exchange coverage provisions-including any applicable PDLs (Preferred Drug Lists)-conflict with the coverage provisions in this drug policy, health plan Exchange coverage provisions take precedence per the Preferred Drug Guidelines OR

3. For Health Plans that utilize NCH UM Oncology Clinical Policies as the initial clinical criteria, the Preferred Drug Guidelines shall follow NCH L1 Pathways when applicable, otherwise shall follow NCH drug policies AND
4. Continuation requests of previously approved, non-preferred medication are not subject to this provision AND
5. When applicable, generic alternatives are preferred over brand-name drugs.

B. Classical Hodgkin Lymphoma

1. NOTE 1: The preferred regimen for first line therapy in stage III and IV classical Hodgkin's Lymphoma, per NCH Policies and NCH Pathways, is ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) except in members with contraindications or intolerance to Bleomycin (e.g., lung disease, prior smoking history) AND IPS- International Prognostic Score of 2-7 (see below). This recommendation is based on the lack of Level 1 evidence (randomized trials and or meta-analyses) to show that Adcetris (brentuximab) + AVD has an overall survival advantage over ABVD for the risk categories other than those above (e.g., lung disease, prior smoking history).
2. NOTE 2: Per NCH pathway & NCH policy, the combination of [Adcetris (brentuximab) + Opdivo (nivolumab)] is a non-preferred regimen post-transplant or, if transplant ineligible, for relapsed/refractory Hodgkin Lymphoma due to the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) to show superior outcomes compared to the NCH Preferred regimens. Please refer to NCH L1 pathway for the preferred treatments for relapsed/refractory Hodgkin Lymphoma.
3. Adcetris (brentuximab vedotin) is being used in member with classical Hodgkin Lymphoma that is CD-30 positive and the following:
    a. Primary treatment in combination with AVD (doxorubicin, vinblastine, dacarbazine) for unfavorable stage I-II or stage III-IV disease in members who have a contraindication to the use of Bleomycin OR
    b. As a single agent for subsequent lines of therapy OR
    c. As consolidation therapy in members who have not received prior brentuximab vedotin following HSCT (Hematopoietic Stem Cell Transplant).

International Prognostic Score in Hodgkin Lymphoma

- ☐ Serum Albumin <4 g/dL (1 point)
- ☐ Hemoglobin <10.5 g/dL (1 point)
- ☐ Male Sex (1 point)
- ☐ Stage IV Disease by Ann Arbor Classification (1 point)
- ☐ Age ≥45 Years (1 point)
- ☐ White Cell Count ≥15,000/mm3 (1 point)

☐ Lymphocyte Count <600/mm3 or <8% of White Cell Count (1 point)

IPS Score: 5 year Freedom From Progression (FFP) and Overall Survival (OS)

0 Points:	84% Freedom from progression and 89% overall survival
1 Point:	77% Freedom from progression and 90% overall survival
2 Points:	67% Freedom from progression and 81% overall survival
3 Points:	60% Freedom from progression and 78% overall survival
4 Points:	51% Freedom from progression and 61% overall survival
5 to 7 Points:	42% Freedom from progression and 56% overall survival

Bottom of Form

C. CD-30 Positive T-Cell Lymphomas

1. Adcetris (brentuximab vedotin) is being used for T-Cell Lymphomas (including anaplastic large cell lymphomas) that are CD30 positive and any of the following:
   a. First line therapy as a single agent or as a component of brentuximab vedotin + chemotherapy [e.g., CHP (cyclophosphamide, doxorubicin, prednisone)] OR
   b. Second line or subsequent therapy as a single agent for relapsed/refractory disease.

III. EXCLUSION CRITERIA

A. Disease progression while on Adcetris (brentuximab vedotin).

B. Dosing exceeds single dose limit of Adcetris (brentuximab vedotin) 180 mg (1.8 mg/kg/dose) or 120 mg (1.2 mg/kg/dose).

C. Treatment with Adcetris (brentuximab vedotin) exceeds the maximum duration limit of 6 month cycles as a part of AAVD (12 doses for first line treatment of Hodgkin's Disease) OR exceeds 16 cycles for refractory/relapsed disease/consolidation treatment after HSCT OR exceeds 8 doses for previously untreated CD-30 + T Cell Lymphoma.

D. Investigational use of Adcetris (brentuximab vedotin) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
   1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.

2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of < 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

B. Requests for Adcetris (brentuximab vedotin) shall be reviewed for appropriateness per FDA approved product.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. Hasenclever D, Diehl V. A prognostic score for advanced Hodgkin's disease. International Prognostic Factors Project on Advanced Hodgkin's Disease. N Engl J Med. 1998 Nov 19;339(21):1506-14.

B. Connors JM, et al. ECHELON-1 Study Group. Brentuximab Vedotin with Chemotherapy for Stage III or IV Hodgkin's Lymphoma. N Engl J Med. 2018 Jan 25;378(4):331-344.

C. Horwitz S, et al. ECHELON-2 Study Group. Brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma (ECHELON-2): a global, double-blind, randomised, phase 3 trial. Lancet. 2019 Jan 19;393(10168):229-240.

D. Adcetris prescribing information. Seagen Inc. Bothell, WA 2021.

E. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

F. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.