



Drug Policy:

Bevacizumab Products

POLICY NUMBER UM ONC_1028	SUBJECT Bevacizumab Products: Avastin™ (bevacizumab)/ Mvasi™(bevacizumab-awwb)/Zirabev™ (bevacizumab-bvzr) Alymsys™ (bevacizumab- maly), Vegzelma (bevacizumab-adcd)		DEPT/PROGRAM UM Dept	PAGE 1 of 6
DATES COMMITTEE REVIEWED 11/04/10, 10/05/11, 02/08/12, 10/13/13, 12/03/14, 01/19/15, 04/13/16, 02/06/17, 10/11/17, 09/21/18, 07/10/19, 09/11/19, 12/11/19, 01/08/20, 02/12/20, 03/11/20, 07/08/20, 07/14/21, 10/13/21, 11/15/21, 12/08/21, 01/12/22, 03/09/22, 05/11/22, 06/08/22, 07/13/22, 09/14/22, 11/09/22, 12/14/22, 03/08/23, 04/12/23, 06/14/23	APPROVAL DATE June 14, 2023	EFFECTIVE DATE June 30, 2023	COMMITTEE APPROVAL DATES 11/04/10, 10/05/11, 02/08/12, 10/13/13, 12/03/14, 01/19/15, 04/13/16, 02/06/17, 10/11/17, 09/21/18, 07/10/19, 09/11/19, 12/11/19, 01/08/20, 02/12/20, 03/11/20, 07/08/20, 07/14/21, 10/13/21, 11/15/21, 12/08/21, 01/12/22, 03/09/22, 05/11/22, 06/08/22, 07/13/22, 09/14/22, 11/09/22, 12/14/22, 03/08/23, 04/12/23, 06/14/23	
PRIMARY BUSINESS OWNER: UM			COMMITTEE/BOARD APPROVAL Utilization Management Committee	
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 Bevacizumab Products: Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr)/Alymsys (bevacizumab-maly)/Vegzelma (bevacizumab-adcd) 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. Continuation requests for a not-approvable medication shall be exempt from this NCH policy provided:

1. The requested medication was used within the last year, **AND**
2. The member has not experienced disease progression and/or no intolerance to the requested medication, **AND**
3. Additional medication(s) are not being added to the continuation request.

B. Brain Necrosis

1. Bevacizumab/bevacizumab biosimilar may be used as monotherapy for members with brain necrosis or edema due to cranial irradiation. Use of bevacizumab/bevacizumab biosimilar is not recommended in members with intracranial hemorrhage.

C. Cervical Cancer

1. For members with metastatic/recurrent/unresectable cervical cancer with tumor PD-L1 staining showing a CPS of less than 1%, bevacizumab/bevacizumab biosimilar may be used as first line/initial therapy in any one of the following regimens:
 - a. In combination with cisplatin/carboplatin + paclitaxel
 - b. In combination with topotecan + paclitaxel.
2. **NOTE:** [Bevacizumab/bevacizumab biosimilar + Keytruda (pembrolizumab) + cisplatin/carboplatin + paclitaxel] is not supported by NCH Policy for initial treatment of PD-L1 positive (PD-L1 greater than or equal to 1%) metastatic cervical cancer. The above policy position is based on the results of KEYNOTE-826 trial referenced below. This trial showed no overall survival benefit from adding bevacizumab to [platinum + paclitaxel + pembrolizumab] in PD-L1 positive patients with metastatic/recurrent/inoperable cervical carcinoma. Please refer to the NCH recommended alternatives agents/regimens, including but not limited to regimens at <http://pathways.newcenturyhealth.com>.

D. Colorectal Cancer

1. The member has unresectable advanced or metastatic colorectal cancer and bevacizumab/bevacizumab biosimilar is being used as **ONE** of the following:
 - a. As initial therapy in combination with capecitabine or with FOLFOX, FOLFIRI, FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin), 5-FU/LV (fluorouracil and leucovorin), or CapeOX (capecitabine and oxaliplatin).
 - b. As subsequent line of therapy given in combination with FOLFOX, FOLFIRI, XELIRI, and XELOX/CapeOX.
 - c. Bevacizumab/bevacizumab biosimilar may be used for up to 2 lines of therapy in the metastatic setting or up to 3 lines of therapy for bevacizumab/bevacizumab biosimilar + Lonsurf (trifluridine and tipiracil)

E. Glioblastoma

1. The member has glioblastoma, anaplastic astrocytoma, or high-grade glioma and bevacizumab/bevacizumab biosimilar is being used as a single agent **OR**
2. Bevacizumab/bevacizumab biosimilar may be used in combination with irinotecan, carboplatin, carmustine, lomustine, or temozolomide for recurrent glioblastoma, anaplastic astrocytoma, or high-grade glioma.

F. Hepatocellular Carcinoma

1. The member has metastatic/inoperable/advanced hepatocellular carcinoma (Child-Pugh Class A or B) and bevacizumab/bevacizumab biosimilar will be used in combination with Tecentriq (atezolizumab) for initial therapy.

G. Non-Small Cell Lung Cancer (NSCLC)

1. Bevacizumab/bevacizumab biosimilar based regimens are not supported by NCH Policy. This Policy position is based on:
 - a. Lack of data supporting the use of such regimens in 2nd line or later lines of therapy, and
 - b. Increased risk of serious adverse effects, and
 - c. Marginal PFS and OS benefit in the first line setting as shown in randomized trials (e.g., a 2 month OS benefit and a 1.3 month PFS benefit with 15 treatment related deaths in the bevacizumab arm including 5 from pulmonary hemorrhage, please see reference).
 - d. Alternative agents/regimens recommended by NCH can be found at: <http://pathways.newcenturyhealth.com>.
2. NOTE: [Bevacizumab/bevacizumab biosimilar + Tarceva (erlotinib)] is not supported by NCH policy for the treatment of metastatic Non-Small Cell Lung Cancer. The above Policy Position is based on the lack of Level 1 evidence (randomized trials and or meta-analyses) to show superior outcomes with the above regimen compared to NCH recommended alternatives agents/regimens, including but not limited to regimens at <http://pathways.newcenturyhealth.com>.

H. Ovarian Cancer

1. The member has recurrent or metastatic ovarian cancer and bevacizumab/bevacizumab biosimilar may be used in any of the following clinical settings:
 - a. For initial/first line therapy of stage II- IV, with chemotherapy.
 - b. For maintenance therapy after complete/partial response to primary chemotherapy + bevacizumab/bevacizumab biosimilar, for stage II-IV disease as follows:
 - i. As monotherapy for BRCA 1 or 2 Wild-Type or Unknown, HRD negative (Homologous Recombination Deficiency negative) or HRD unknown OR
 - ii. In combination with Lynparza (olaparib) for BRCA 1 or 2 mutation (germline or somatic) or HRD positive.
2. For therapy of relapsed/recurrent ovarian cancer, bevacizumab/bevacizumab biosimilar may be used as monotherapy or with chemotherapy.

I. Renal Cell Carcinoma

1. Bevacizumab/bevacizumab biosimilars are not supported by NCH Policy for use in metastatic renal cell carcinoma. The above policy position is based on the lack of Level 1 evidence (randomized trials and/or meta-analyses) to superior outcomes with bevacizumab/bevacizumab biosimilar in comparison to alternative agents/regimens that can be found at: <https://pathway.newcenturyhealth.com>.

III. EXCLUSION CRITERIA

- A. Bevacizumab/bevacizumab biosimilar is being used on or after disease progression on a bevacizumab containing regimen; except in colorectal cancer, bevacizumab may be used up to 2 lines of therapy in the metastatic setting or up to 3 lines of therapy for bevacizumab /bevacizumab biosimilar + Lonsurf (trifluridine and tipiracil).
- B. Members with Child-Pugh Class B or C hepatocellular carcinoma.

- C. Dosing exceeds single dose limit of bevacizumab/bevacizumab biosimilar 15 mg/kg. Per NCH Policy, the maximum dose of bevacizumab when used in combination with irinotecan/FOLFIRI/FOLOX/IROX regimen is 5 mg/kg.
- D. For Brain Necrosis: Treatment exceeds the maximum duration limit of 4 doses (dose range from 5 mg/kg every 2 weeks to 7.5 mg/kg every 3 weeks).
- E. Investigational use of bevacizumab products 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 definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
 - 4. Whether the experimental design, considering 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.

V. APPROVAL AUTHORITY

- A. Review – Utilization Management Department
- B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

- A. None

VII. REFERENCES

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