# Drug Policy:

# Avastin™ (bevacizumab)/ Mvasi™(bevacizumab-awwb)/ Zirabev™ (bevacizumab-bvzr)

| | | | | |
|---|---|---|---|---|
| **POLICY NUMBER**<br>UM ONC_1028 | **SUBJECT**<br>Avastin™ (bevacizumab)/ Mvasi™(bevacizumab-awwb)/ Zirabev™ (bevacizumab-bvzr) | | **DEPT/PROGRAM**<br>UM Dept | **PAGE 1 of 5** |
| **DATES COMMITTEE REVIEWED**<br>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 | **APPROVAL DATE**<br>November 15, 2021 | **EFFECTIVE DATE**<br>November 29, 2021 | **COMMITTEE APPROVAL DATES**<br>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 | |
| **PRIMARY BUSINESS OWNER:** UM | | **COMMITTEE/BOARD APPROVAL**<br>Utilization Management Committee | | |
| **URAC STANDARDS**<br>HUM 1 | **NCQA STANDARDS**<br>UM 2 | | **ADDITIONAL AREAS OF IMPACT** | |
| **CMS REQUIREMENTS** | **STATE/FEDERAL REQUIREMENTS** | | **APPLICABLE LINES OF BUSINESS**<br>Commercial, Exchange, Medicaid | |

## I. PURPOSE

To define and describe the accepted indications for Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) 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.
6. Mvasi (bevacizumab-awwb) and Zirabev (bevacizumab-bvzr) are the PREFERRED products whenever Bevacizumab is requested AND
7. Non-preferred Bevacizumab will be approved only if there is a contraindication or intolerance to the PREFERRED medication.

## B. Colorectal Cancer

1. The member has unresectable advanced or metastatic colorectal cancer and Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) is being used as ONE of the following:
   a. As initial therapy in combination with capecitabine or with FOLFOX, FOLFIRI, FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan), 5-FU/LV (fluorouracil and leucovorin), or CapeOX (capecitabine and oxaliplatin).
   b. As subsequent therapy after progression on a prior non-bevacizumab based regimen, given in combination with FOLFOX, FOLFIRI, XELIRI, and XELOX/CapeOX.
   c. Bevacizumab may be used in a maximum of 2 lines of therapy, in the metastatic setting.

## C. Non-Small Cell Lung Cancer (NSCLC)

1. NOTE: Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) are non-preferred per NCH Policy & NCH Pathway for metastatic non-squamous Non-Small Cell Lung Cancer. Please refer to the NCH Pathway document for the current recommended regimens in the above cancer type/stage.

## D. Glioblastoma

1. The member has glioblastoma, anaplastic astrocytoma, or high-grade glioma and Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) is being used as a single agent or in combination with irinotecan, carmustine, lomustine, or temozolomide, in any line of therapy for this disease.

## E. Renal Cell Carcinoma

1. NOTE: Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) is a non-preferred drug for metastatic clear cell renal cell carcinoma.
2. The member has recurrent or metastatic disease and Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) is being used as ONE of the following:
   a. As single agent for members who have experienced disease progression on an oral TKI (e.g., pazopanib) AND an Immune Checkpoint Inhibitor (e.g., pembrolizumab) for clear cell histology

b. A single agent for non-clear cell histology, in any line of therapy.

## F. Cervical Cancer

1. NOTE: Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) + Cisplatin/Carboplatin + Paclitaxel is the preferred regimen for initial/first line therapy for metastatic cervical carcinoma.
2. The member has cervical cancer and Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) is being used as first line therapy in combination with paclitaxel and cisplatin/carboplatin or topotecan for local/regional recurrence or distant metastases.

## G. Hepatocellular Carcinoma

1. NOTE: Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) + Tecentriq (atezolizumab) is the preferred regimen for initial/first line therapy for unresectable/ metastatic hepatocellular carcinoma (Child-Pugh Class A only).
2. Member has metastatic/inoperable/advanced hepatocellular carcinoma (Child-Pugh Class A only) and Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) will be used in combination with Tecentriq (atezolizumab) for initial therapy.

## H. Ovarian Cancer

NOTE: Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) is non-preferred in the treatment of ovarian cancer. This recommendation is based on a lack of Level 1 evidence (randomized trials and or meta-analyses) to show an overall survival (OS) advantage with Bevacizumab + Chemotherapy over other alternative chemotherapy regimens on NCH L1 pathway for adjuvant, recurrent, or metastatic treatment of ovarian cancer. A summary of the original trials to support this recommendation is as follows:

Primary setting after debulking surgery:

1. GOG 218: Extended long term follow-up data at 103 months (7 years beyond the primary analysis) continued to report no difference among the groups in terms of OS. The median OS was 43.8 months with bevacizumab + chemotherapy followed by bevacizumab, compared with 40.6 months with chemotherapy alone (HR, 0.89; 95% CI, 0.76-1.05). The median OS with bevacizumab plus chemotherapy followed by placebo was 38.8 months (HR of 1.06 vs chemotherapy alone, 95% CI, 0.90-1.24).[A]
2. ICON 7: At a median follow-up of 49 months, an updated analysis of PFS showed no difference between treatment (17 versus 20 months; HR 0.93, 95% CI 0.83-1.0, p= 0.25), and more serious grade 3/4 adverse events (3 versus 7 percent), including a higher rate of mild to serious grade 2 or higher hypertension (2 versus 18 percent). Grade 3 or worse gastrointestinal perforations occurred in 10 patents (1%). There was no difference in overall survival or QOL.[B]

Second line and salvage settings (platinum sensitive)

1. OCEANS: At a median follow-up of 42 months, overall survival data did not mature but the trial noted an improved progression-free survival benefit of 4 months (8.4 vs 12.4 months; HR = 0.484 95% CI 0.39-0.60, p= < 0.0001). There was no improvement in OS with bevacizumab when added to concurrent chemotherapy. [C, D]
2. GOG 213: At a median follow up of 50 months, there was 4 months improvement in PFS, 14 vs 10 months. The median overall survival in the chemotherapy plus bevacizumab group was 42 months (95% CI 37·7-46·2) versus 37 months (32·6-39·7) in the chemotherapy group with an adjusted HR of 0.823 (95% CI 0·680-0·996; p=0·0447). The adjustment in the HR was due to incorrect stratification of treatment free interval in 7% of patients. The data for the

effect of secondary cytoreduction on OS has not been reached and was not reported in the analysis. [E]

Second line and salvage settings (platinum resistant)

1. AURELIA: At a median follow-up of 13 months, the administration of the bevacizumab with chemotherapy was associated with a PFS benefit of 2.7 months (3.4 vs 6.7 months HR= 0.48 95% CI, 0.38 to 0.60, p= <0.001). There was no improvement in OS with bevacizumab when added to concurrent chemotherapy. Grade 2 hypertension and proteinuria were more common with bevacizumab. GI perforation occurred in 2.2% of bevacizumab-treated patients. [F]

## III. EXCLUSION CRITERIA

A. Members with Child-Pugh Class B or C hepatocellular carcinoma.

B. Dosing exceeds single dose limit of Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) 15 mg/kg. Per NCH L1 Pathway, the maximum dose of Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) when used in combination with irinotecan/FOLFIRI/FOLOX/IROX regimen is 5 mg/kg.

C. Investigational use of Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) 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.

## V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

## VI. ATTACHMENTS

A. None

## VII. REFERENCES


A. Burger RA. et al. Independent radiologic review of the Gynecologic Oncology Group Study 0218, a phase III trial of bevacizumab in the primary treatment of advanced epithelial ovarian, primary peritoneal, or fallopian tube cancer. Gynecol Oncol. 2013 Oct;131(1):21-6.

B. Oza AM, et al. Standard chemotherapy with or without bevacizumab for women with newly diagnosed ovarian cancer (ICON7): overall survival results of a phase 3 randomised trial. Lancet Oncol. 2015 Aug;16(8):928-36.

C. Aghajanian C, et al. OCEANS: a randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Clin Oncol. 2012 Jun 10;30(17):2039-45.

D. Aghajanian C, Goff B, Nycum LR, Wang YV, Husain A, Blank SV. Final overall survival and safety analysis of OCEANS, a phase 3 trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent ovarian cancer. Gynecol Oncol. 2015;139(1):10–16.

E. Coleman RL, et al. Bevacizumab and paclitaxel-carboplatin chemotherapy and secondary cytoreduction in recurrent, platinum-sensitive ovarian cancer (NRG Oncology/Gynecologic Oncology Group study GOG-0213): a multicentre, open-label, randomised, phase 3 trial. Lancet Oncol. 2017;18(6):779–791.

F. Pujade-Lauraine E, et al. Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer: The AURELIA open-label randomized phase III trial. J Clin Oncol. 2014 May 1;32(13):1302-8.

G. Avastin Product Information. Genentech, Inc. South San Francisco, CA 2021.

H. Mvasi Product Information. Amgen, Inc. Thousand Oaks, CA 2021.

I. Zirabev Product Information. Pfizer, Laboratories Div Pfizer Inc NY, NY 2021.

J. Clinical Pharmacology Elsevier Gold Standard 2021.

K. Micromedex Healthcare Series: Thomson Micromedex, Greenwood Village, CO 2021.

L. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2021.

M. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2021.

N. 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.

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