Evolent Clinical Guideline 3154 for Bevacizumab Products

Guideline Number:	Applicable Codes	
Evolent_CG_3154		
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STATEMENT

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)/Avzivi (bevacizumab-tnjn)/Jobevne (bevacizumab-nwgd) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent 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.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Brain Necrosis

- 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.

Cervical Cancer

- For members with metastatic/recurrent/unresectable cervical cancer, bevacizumab/bevacizumab biosimilar may be used as first line/initial therapy in any one of the following regimens:
  - In combination with cisplatin/carboplatin + paclitaxel
  - In combination with topotecan + paclitaxel.
- Bevacizumab/bevacizumab biosimilar + Keytruda (pembrolizumab) + cisplatin/carboplatin + paclitaxel may be used in members for the initial treatment of PD-

L1 positive (PD-L1 greater than or equal to 1%) metastatic cervical cancer.

Colorectal Cancer

- The member has unresectable advanced or metastatic colorectal cancer and bevacizumab/bevacizumab biosimilar is being used as ONE of the following:
  - 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).
  - As subsequent line of therapy given in combination with FOLFOX, FOLFIRI, XELIRI, and XELOX/CapeOX.
  - 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)

Glioblastoma

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

Hepatocellular Carcinoma

- Bevacizumab/bevacizumab biosimilar may be used in combination with Tecentriq (atezolizumab) as adjuvant therapy in adult members with hepatocellular carcinoma (Child-Pugh Class A), following resection or ablation, who are at high risk of recurrence.
  - High risk of recurrence is defined by any of the following:
    - Tumor size > 5 cm
    - Member having > 3 tumors
    - Macrovascular invasion or microvessel invasion on histology
    - Grade 3/4 histology
- The member has metastatic/inoperable/advanced hepatocellular carcinoma (Child-Pugh Class A) and bevacizumab/bevacizumab biosimilar will be used in combination with Tecentriq (atezolizumab) for initial therapy.

Non-Small Cell Lung Cancer (NSCLC)

- Bevacizumab/bevacizumab biosimilar may be used in combination with atezolizumab, paclitaxel, and carboplatin, for the first-line treatment of adult members with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations.
- NOTE: Per Evolent Policy, the following regimens are not supported for the treatment of

metastatic NSCLC based on the lack of Level 1 evidence (randomized trials and or meta-analyses) to show superior outcomes compared to Evolent recommended alternatives agents/regimens, including but not limited to regimens at **Evolent Pathways**:

- Bevacizumab/bevacizumab biosimilar + Tarceva (erlotinib)
- Bevacizumab/bevacizumab biosimilar + Carboplatin/Cisplatin + Pemetrexed followed by maintenance Bevacizumab/bevacizumab biosimilar + Pemetrexed

Ovarian Cancer

- The member has recurrent or metastatic ovarian cancer and bevacizumab/bevacizumab biosimilar may be used in any of the following clinical settings:
  - For initial/first line therapy of stage II- IV, with chemotherapy.
  - For maintenance therapy after complete/partial response to primary chemotherapy + bevacizumab/bevacizumab biosimilar, for stage II-IV disease as follows:
    - As monotherapy for BRCA 1 or 2 Wild-Type or Unknown, HRD negative (Homologous Recombination Deficiency negative) or HRD unknown OR
    - In combination with Lynparza (olaparib) for BRCA 1 or 2 mutation (germline or somatic) or HRD positive.
- For therapy of relapsed/recurrent ovarian cancer, bevacizumab/bevacizumab biosimilar may be used as monotherapy or with chemotherapy.
- Bevacizumab/bevacizumab biosimilar may be used in combination with Keytruda (pembrolizumab) and paclitaxel for the treatment of adult members with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal carcinoma whose tumors express PD-L1 (CPS ≥1) as determined by an FDA authorized test, and who have received one or two prior systemic treatment regimens.

Renal Cell Carcinoma

- NOTE: Bevacizumab/bevacizumab biosimilars are not supported by Evolent 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 **Evolent Pathways.**

CONTRAINDICATIONS/WARNINGS

- Warnings
  - Surgery and Wound Healing Complications
    - In patients who experience wound healing complications during bevacizumab treatment, withhold bevacizumab until adequate wound healing. Withhold for at least 28 days prior to elective surgery. Do not administer bevacizumab for at

least 28 days following a major surgery, and until adequate wound healing. The safety of resumption of bevacizumab after resolution of wound healing complication has not been established. Discontinue for wound healing complication of necrotizing fasciitis.

EXCLUSION CRITERIA

- Bevacizumab/bevacizumab biosimilar is being used on or after disease progression on a bevacizumab containing regimen; except in colorectal cancer, bevacizumab/bevacizumab biosimilar 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).
- Members with Child-Pugh Class B or C hepatocellular carcinoma.
- Dosing exceeds single dose limit of bevacizumab/bevacizumab biosimilar 15 mg/kg. Per Evolent Policy, the maximum dose of bevacizumab when used in combination with irinotecan/FOLFIRI/FOLFOX/IROX regimen is 5 mg/kg.
- 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).
- 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:
    - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
    - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
    - 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.
    - 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).
    - 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.
    - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
    - 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.

CODING AND STANDARDS

Codes

- C9257 - Injection, bevacizumab, 0.25 mg
- J9035 - Injection, bevacizumab, 10 mg
- Q5107 - Injection, bevacizumab-awwb, biosimilar, (mvasi), 10 mg
- Q5118 - Injection, bevacizumab-bvzr, biosimilar, (zirabev), 10 mg
- Q5126 - Injection, bevacizumab-maly, biosimilar, (alymsys), 10 mg
- Q5129 - Injection, bevacizumab-adcd (vegzelma), biosimilar, 10 mg
- Q5160 - Injection, bevacizumab-nwgd (jobevne), biosimilar, 10 mg
- J9999 - bevacizumab-tnjn

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
August 2026	• Updated ovarian cancer indication • Updated HCPC code • Updated references
August 2025	• Removed PD-L1 requirement when used in combination with paclitaxel + cisplatin/carboplatin or paclitaxel + topotecan for initial line, metastatic/recurrent/unresectable cervical cancer to match compendia
July 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1028 Bevacizumab Products • Added verbiage to NSCLC indication section that states that bevacizumab + carboplatin/cisplatin + pemetrexed followed by maintenance bevacizumab + pemetrexed is not supported by Evolent Policy • Updated indication section • Added new biosimilar product “Jobevne (bevacizumab-nwgd)” to policy • Updated exclusion criteria • Updated references
November 2024	• Updated HCC indication section to include adjuvant treatment in combination with atezolizumab in adult members with high risk of recurrence • Added criteria for high risk of recurrence • Updated references
June 2024	• Added to NSCLC indication section: “Bevacizumab/bevacizumab biosimilar may be used in combination with atezolizumab, paclitaxel, and carboplatin, for the first-line treatment of adult members with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations.” • Added new reference

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

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