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Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), bevacizumab-bvzr (Zirabev®)

Prior Authorization Drug Coverage Policy

Effective Date: 12/15/2020
Revision Date: n/a
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Lines of Business: Commercial
Policy type: Prior Authorization

This Drug Coverage Policy provides parameters for the coverage of bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), bevacizumab-bvzr (Zirabev®). Consideration of medically necessary indications are based upon U.S. Food and Drug Administration (FDA) indications, recommended uses within the Centers of Medicare & Medicaid Services (CMS) five recognized compendia, including the National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium (Category 1 and 2A recommendations), and peer-reviewed scientific literature eligible for coverage according to the CMS, Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 titled, "Off-Label Use of Anti-Cancer Drugs and Biologics." This policy evaluates whether the drug therapy is proven to be effective based on published evidence-based medicine.

Drug Description[1-3]

Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), and bevacizumab-bvzr (Zirabev®) bind to vascular endothelial growth factor (VEGF) and prevent the interaction of VEGF to its receptors Fms-like tyrosine kinase-1 (Flt-1) and kinase insert domain receptor (KDR) on the surface of endothelial cells. The interaction of VEGF with its receptors leads to endothelial cell proliferation and new blood vessel formation in invitro models of angiogenesis. Administration of bevacizumab, bevacizumab-awwb, and bevacizumab-bvzr to xenotransplant models of colon cancer in nude (athymic) mice caused reduction of microvascular growth and inhibition of metastatic disease progression.

Bevacizumab-awwb and bevacizumab-bvzr are FDA approved biosimilar products to bevacizumab.

FDA Indications[1-3]

Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), and bevacizumab-bvzr (Zirabev®) are FDA indicated for the following:

- **Cervical cancer, persistent/recurrent/metastatic**: in combination with paclitaxel and either cisplatin or topotecan.

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- **Metastatic colorectal cancer**: initial or subsequent treatment of metastatic colorectal cancer in combination with fluorouracil-based chemotherapy **OR** in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab-containing regimen
- **Recurrent glioblastoma**.
- **Non-small cell lung cancer, non-squamous**: first-line treatment of unresectable, locally advanced, recurrent or metastatic disease in combination with carboplatin and paclitaxel.
- **Metastatic renal cell carcinoma**: in combination with interferon alfa.

Bevacizumab (Avastin®) is also FDA indicated for the following:

- **Hepatocellular carcinoma, unresectable or metastatic**
- **Ovarian (epithelial), fallopian tube, or primary peritoneal cancer**:
    - Stage III or IV disease, following initial surgical resection: in combination with carboplatin and paclitaxel, followed by single-agent bevacizumab.
    - Platinum-resistant recurrent: in combination with paclitaxel, doxorubicin (liposomal), or topotecan in patients who received no more than 2 prior chemotherapy regimens.
    - Platinum-sensitive recurrent: in combination with carboplatin and paclitaxel or with carboplatin and gemcitabine and then followed by single-agent bevacizumab.
    - Note that the use of Mvasi® and Zirabev® are not FDA indicated for patients with ovarian, fallopian tube, or primary peritoneal cancer.

NCCN Compendium Supported Indications (Avastin®)[1-4]

- Breast cancer.
- Central nervous system cancers.
- Cervical cancer.
- Colon cancer.
- Hepatobiliary cancers.
- Kidney cancer.
- Malignant pleural mesothelioma
- Non-small cell lung cancer.
- Ovarian cancer/fallopian tube cancer/primary peritoneal cancer.
- Rectal cancer
- Small bowel adenocarcinoma.
- Soft tissue sarcoma.
- Uterine neoplasms.
- Vulvar cancer.

NCCN Compendium Supported Indications (Mvasi, Zirabev)[1-4]

- Breast cancer
- Central nervous system cancers.
- Cervical cancer.
- Colon cancer

- Hepatobiliary cancers.
- Kidney cancer.
- Malignant pleural mesothelioma.
- Non-small cell lung cancer.
- Ovarian cancer/fallopian tube cancer/primary peritoneal cancer.
- Rectal cancer.
- Uterine neoplasms.
- Vulvar cancer.

Coverage Determinations[1-4]

Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), and bevacizumab-bvzr (Zirabev®) will require prior authorization. These agents are considered medically necessary for members with the following oncology indications when all criteria are met:

Cervical cancer:

- Member has a diagnosis of stage IVB cervical cancer **OR** has distant metastases **OR** has local/regional recurrence **AND**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as first-line therapy **OR** second-line therapy as clinically appropriate (if not used previously as first-line) in combination with paclitaxel and cisplatin or carboplatin, **OR** in combination with paclitaxel and topotecan

Recommended dosage: 15 mg/kg IV every 21 days.

Colon cancer:

- Member has a diagnosis of colon cancer **AND**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used in combination with capecitabine or with 5-fluorouracil (5-FU)/leucovorin in patients not candidates for intensive therapy as any of the following:
    - primary treatment for locally unresectable or medically inoperable disease
    - for unresectable synchronous liver and/or lung metastases that remain unresectable after primary systemic therapy
    - as primary treatment for synchronous abdominal/peritoneal metastases that are non-obstructing, or following local therapy for patients with existing or imminent obstruction
    - for synchronous unresectable metastases of other sites
    - as primary treatment for unresectable metachronous metastases in patients who have not received previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine/oxaliplatin) within the past 12 months, who have received previous 5-FU/leucovorin or capecitabine therapy, or who have not received any previous chemotherapy
    - for unresectable metachronous metastases that remain unresectable after primary treatment **OR**

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- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as subsequent therapy for progression of advanced or metastatic disease as any of the following:
    - in combination with irinotecan or FOLFIRI (fluorouracil, leucovorin, and irinotecan) if previously treated with oxaliplatin-based therapy without irinotecan
    - in combination with FOLFOX or CapeOX if previously treated with irinotecan-based therapy without oxaliplatin
    - in combination with irinotecan or FOLFIRI if previously treated with fluoropyrimidine therapy without irinotecan or oxaliplatin
    - in combination with FOLFOX, CapeOX, or irinotecan and oxaliplatin if previously treated with fluoropyrimidine therapy without irinotecan or oxaliplatin **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as primary treatment (either in combination with irinotecan or FOLFIRI) for patients with unresectable metachronous metastases and previous adjuvant FOLFOX or CapeOX within the past 12 months **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as primary treatment for unresectable synchronous liver and/or lung metastases in combination with FOLFOX, FOLFIRI, FOLFOXIRI, or CapeOx **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used in combination with FOLFOX, FOLFIRI, CapeOX, or FOLFOXIRI (5-FU, leucovorin, oxaliplatin, irinotecan) in candidates for intensive therapy as any of the following:
    - as primary treatment for locally unresectable or medically inoperable disease
    - for unresectable synchronous liver and/or lung metastases that remain unresectable after primary systemic therapy
    - as primary treatment for synchronous abdominal/peritoneal metastases that are non-obstructing, or following local therapy for patients with existing or imminent obstruction
    - for synchronous unresectable metastases of other sites
    - as primary treatment for unresectable metachronous metastases in patients who have not received previous adjuvant FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin or capecitabine therapy, or who have not received any previous chemotherapy
    - for unresectable metachronous metastases that remain unresectable after primary treatment
    - and progressed on non-intensive therapy, except if received previous fluoropyrimidine, with improvement in functional status

Recommended dosage: doses vary from 5-10 mg/kg IV every 14 days or 7.5 mg/kg IV every 21 days. Note that bevacizumab 10 mg/kg is utilized with the FOLFOX4 regimen.

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Rectal cancer:

- Member has a diagnosis of rectal cancer **AND**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as primary treatment (either in combination with irinotecan or FOLFIRI) for patients with unresectable metachronous metastases and previous adjuvant FOLFOX or CapeOX within the past 12 months **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as primary treatment for unresectable synchronous liver and/or lung metastases in combination with FOLFOX, FOLFIRI, FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan), or CapeOx **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as primary treatment for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable or medically inoperable disease if resection is contraindicated following neoadjuvant therapy in patients appropriate for intensive therapy in CapeOx, FOLFOX, or FOLFIRI **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as primary treatment for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable or medically inoperable disease if resection is contraindicated following neoadjuvant therapy in patients not appropriate for intensive therapy in combination with capecitabine or 5-FU/leucovorin **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used in combination with capecitabine or 5-FU/leucovorin in patients not appropriate for intensive therapy as any of the following:
    - for synchronous liver or lung metastases that are unresectable or medically inoperable and remain unresectable (with no progression of primary tumor) after primary systemic therapy
    - following palliative radiation therapy or chemo/radiation for synchronous liver or lung metastases that are unresectable or medically inoperable and remain unresectable (with progression of primary tumor) after primary systemic therapy
    - as primary treatment for synchronous abdominal/peritoneal metastases that are non-obstructing, or following local therapy for patients with existing or imminent obstruction
    - as primary treatment for synchronous unresectable metastases of other sites
    - as primary treatment for unresectable metachronous metastases in patients who have not received previous adjuvant FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin or capecitabine therapy, or who have not received any previous chemotherapy
    - for unresectable metachronous metastases that remain unresectable after primary treatment **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used combination with FOLFOX, FOLFIRI, CapeOx, or FOLFOXIRI in candidates for intensive therapy as any of the following:

  - for synchronous liver or lung metastases that are unresectable or medically inoperable and remain unresectable (with no progression of primary tumor) after primary systemic therapy
  - following palliative radiation therapy or chemo/radiation for synchronous liver or lung metastases that are unresectable or medically inoperable and remain unresectable (with progression of primary tumor) after primary systemic therapy
  - as primary treatment for synchronous abdominal/peritoneal metastases that are non-obstructing, or following local therapy for patients with existing or imminent obstruction
  - as primary treatment for synchronous unresectable metastases of other sites
  - as primary treatment for unresectable metachronous metastases in patients who have not received previous adjuvant FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin or capecitabine therapy, or who have not received any previous chemotherapy
  - for unresectable metachronous metastases that remain unresectable after primary treatment
  - and progressed on non-intensive therapy, except if received previous fluoropyrimidine, with improvement in functional status **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as subsequent therapy for progression of advanced or metastatic disease as any of the following:
  - in combination with irinotecan or FOLFIRI if previously treated with oxaliplatin-based therapy without irinotecan
  - in combination with FOLFOX or CapeOX if previously treated with irinotecan-based therapy without oxaliplatin
  - in combination with irinotecan or FOLFIRI if previously treated with fluoropyrimidine therapy without irinotecan or oxaliplatin
  - in combination with FOLFOX, CapeOX, or irinotecan and oxaliplatin if previously treated with fluoropyrimidine therapy without irinotecan or oxaliplatin

Recommended dosage: doses vary from 5-10 mg/kg IV every 14 days or 7.5 mg/kg IV every 21 days.

Central nervous system malignancies:

- Member has a diagnosis of meningioma **AND** bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as a single agent **OR**
- Member has brain metastases, metastatic spine tumors, adult intracranial and spinal ependymoma, adult medulloblastoma, adult low-grade (World Health Organization grade II) infiltrative supratentorial astrocytoma/oligodendroglioma, meningiomas, anaplastic gliomas, glioblastoma, or a diagnosis of primary central nervous system lymphoma and bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as a single agent for management of symptoms driven by radiation necrosis, poorly controlled vasogenic edema, or mass effect **OR**

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- Member has a diagnosis of recurrent glioblastoma or anaplastic glioma and bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as a single agent OR in combination with carmustine, lomustine, or temozolomide if bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) monotherapy fails and it is desirable to continue the steroid sparing effects of bevacizumab **OR**
- Member has progressive or recurrent adult intracranial and spinal ependymoma and bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as a single agent **AND** member is refractory to surgery or radiation therapy **AND** any of the following:
    - Gross total or subtotal resection with negative CSF cytology
    - Subtotal resection and evidence of brain, spine, or CSF metastasis
    - Unresectable disease

Recommended dosage: 10 mg/kg IV every 14 days.

Hepatobiliary cancer:

- Member has a diagnosis of hepatobiliary cancer **AND**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is used as first-line treatment in combination with atezolizumab **AND**
- Member has unresectable disease and is not a transplant candidate **OR** is inoperable by performance status or comorbidity, or has local disease or local disease with minimal extrahepatic disease only **OR** has metastatic disease or extensive liver tumor burden

Recommended dosage: 15 mg/kg IV on every 21 days, in combination with atezolizumab.

Non-small cell lung cancer:

- Member has a diagnosis of non-squamous unresectable, locally advanced, recurrent, or metastatic disease **AND**
    - Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as continuation maintenance therapy in patients with performance status 0-2 and no history of recent hemoptysis who achieve tumor response or stable disease following initial systemic therapy as 1) a single agent or 2) in combination with pemetrexed if previously used with a first-line pemetrexed/platinum chemotherapy regimen or 3) in combination with atezolizumab if previously used first-line as part of an atezolizumab/carboplatin/paclitaxel/bevacizumab regimen **OR**
    - Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as continuation maintenance therapy in combination with atezolizumab for PD-L1 expression positive (≥1%) tumors that are EGFR (epidermal growth factor receptor), ALK (anaplastic lymphoma kinase), ROS1, BRAF negative in patients with performance status 0-2 who achieve a response or stable disease following first-line therapy with atezolizumab/carboplatin/paclitaxel/bevacizumab **OR**

- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used in combination with erlotinib for sensitizing EGFR mutation-positive with no history of hemoptysis as: 1) first-line therapy or 2) continuation of therapy following disease progression on combination of erlotinib with bevacizumab for asymptomatic disease, symptomatic brain lesions, or isolated symptomatic systemic lesions **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as first-line therapy for programmed death ligand-1 (PD-L1) expression positive (≥1%) tumors that are EGFR, ALK, ROS1, BRAF negative and performance status 0-2 in combination with atezolizumab, carboplatin and paclitaxel **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used in combination with carboplatin and either paclitaxel or pemetrexed, or in combination with cisplatin and pemetrexed, or in combination with atezolizumab, carboplatin and paclitaxel for in patients with performance status 0-1, and no history of recent hemoptysis as: 1) initial systemic therapy for EGFR, ALK, ROS1, BRAF negative and PD-L1 <1% 2) first-line or subsequent therapy for BRAF V600E-mutation positive tumors 3) first-line (useful in certain circumstances) or subsequent therapy for NTRK gene fusion positive tumors 4) subsequent therapy for sensitizing EGFR mutation-positive tumors and prior erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, or dacomitinib therapy 5) subsequent therapy for ALK rearrangement-positive tumors and prior crizotinib, ceritinib, alectinib, or brigatinib therapy 6) subsequent therapy for ROS1 rearrangement-positive tumors and prior crizotinib, entrectinib, or ceritinib therapy 7) subsequent therapy (except for PD-1/PD-L1 containing regimens) for PD-L1 expression-positive (≥1%) tumors and EGFR, ALK, ROS1, BRAF negative and no prior platinum-doublet chemotherapy but with a PD-1/PD-L1 inhibitor

Recommended dosage: 15 mg/kg IV every 21 days.

Small, fallopian tube, primary peritoneal cancers:

- Member has a diagnosis of ovarian, fallopian tube, or primary peritoneal cancer **AND**:
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used in combination with paclitaxel and carboplatin as primary adjuvant therapy for stage II-IV disease **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used in combination with paclitaxel and carboplatin for patients who are poor surgical candidates or have low likelihood of optimal cytoreduction as: 1) neoadjuvant therapy or 2) continued treatment for stable disease following neoadjuvant therapy or 3) adjuvant therapy following interval debulking surgery in patients with response or stable disease to neoadjuvant therapy **OR**

- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used for rising CA-125 levels or clinical relapse in patients who have received no prior chemotherapy in combination with paclitaxel and carboplatin **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as maintenance therapy for stage II-IV disease if complete clinical remission or partial remission to primary therapy including bevacizumab as: 1) a single agent or in combination with olaparib in patients BRCA1/2 wild-type or unknown or 2) in combination with olaparib in patients with a germline or somatic BRCA1/2 mutation **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used in combination with carboplatin and gemcitabine OR paclitaxel OR liposomal doxorubicin **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as adjuvant treatment in combination with carboplatin and paclitaxel for pathologic stage II-IV, grade 1 endometrioid carcinoma **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as adjuvant treatment for pathologic stage II-IV disease in combination with carboplatin and paclitaxel (for mucinous carcinoma) **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as a single agent for persistent disease or recurrence **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as a single agent for clinical relapse in patients with stage II-IV malignant sex cord-stromal tumors **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used for platinum-resistant persistent disease or recurrence in combination with oral cyclophosphamide, liposomal doxorubicin, weekly paclitaxel, or topotecan **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as adjuvant treatment in combination with carboplatin and paclitaxel for pathologic stage II-IV low-grade serous carcinoma or borderline epithelial tumors with invasive implants **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as targeted therapy in combination with niraparib in platinum-sensitive persistent disease or recurrence **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as maintenance therapy as a single agent if used previously as part of a combination therapy for patients with partial or complete response following recurrence therapy with chemotherapy plus bevacizumab for platinum-sensitive disease

Recommended dosage: 15 mg/kg IV every 21 days.

Renal cell carcinoma:

- Member has a diagnosis of relapsed or metastatic renal cell carcinoma **AND**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is 1) being used in combination with interferon alfa or 2) single-agent systemic therapy for non-clear cell histology or 3) in combination with erlotinib for non-clear cell histology in selected patients with advanced papillary renal cell carcinoma including hereditary leiomyomatosis and renal cell cancer or 4) in combination with everolimus as systemic therapy for non-clear cell histology

Recommended dosage: 10 mg/kg IV every 14 days.

Breast cancer

- Member has a diagnosis of recurrent or stage IV human epidermal growth factor receptor 2 (HER2)-negative breast cancer **AND**
- Bevacizumab is being used in combination with paclitaxel (useful in certain circumstances, in select patients with high tumor burden, rapidly progressing disease, and visceral crisis) for disease that is:
    - hormone receptor-negative **OR**
    - hormone receptor-positive with visceral crisis or endocrine therapy refractory

Recommended dosage: 10 mg/kg IV every 14 days.

Malignant pleural mesothelioma:

- Member has a diagnosis of malignant pleural mesothelioma **AND**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used in patients not eligible for cisplatin in combination with pemetrexed and carboplatin followed by single-agent maintenance bevacizumab as treatment of 1) unresectable clinical stage I-IIIIA disease and epithelioid or biphasic histology or 2) clinical stage IIIB or IV disease, sarcomatoid, or medically inoperable tumors in patients with performance status 0-2 **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used in combination with pemetrexed and cisplatin followed by single-agent maintenance bevacizumab as treatment of: 1) unresectable clinical stage I-IIIIA disease and epithelioid or biphasic histology or 2) clinical stage IIIB or IV disease, sarcomatoid, or medically inoperable tumors in patients with performance status 0-2

Recommended dosage: 15 mg/kg IV every 21 days.

Small bowel adenocarcinoma:

- Member has a diagnosis of advanced or metastatic small bowel adenocarcinoma **AND**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is used as initial therapy in combination with capecitabine or 5-FU/leucovorin **AND** member is not a candidate for intensive therapy **OR**

- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is used as initial therapy in combination with FOLFOX, CapeOx, or FOLFOXIRI **AND** member is a candidate for intensive therapy

Recommended dosage: 1) in combination with FOLFOX OR FOLFOXIRI: 5 mg/kg IV every 14 days 2) in combination with CapeOx: 7.5 mg/kg IV every 21 days.

Soft tissue sarcoma:

- Member has a diagnosis of soft tissue sarcoma **AND**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is used in combination with temozolomide for the treatment of solitary fibrous tumor and hemangiopericytoma **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is used as single agent therapy for angiosarcoma

Recommended dosage: 1) Angiosarcoma: 15 mg/kg IV every 21 days 2) solitary fibrous tumor and hemangiopericytoma: 5 mg/kg IV on days 8 and 22 every 28 days.

Uterine cancers:

- Member has a diagnosis of endometrial cancer **AND**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used in combination with carboplatin and paclitaxel for advanced or recurrent disease only **OR**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used as single agent therapy for disease that has progressed on prior cytotoxic chemotherapy

Recommended dosage: 15 mg/kg IV every 21 days.

Vulvar cancer:

- Member has a diagnosis of vulvar cancer **AND**
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), or bevacizumab-bvzr (Zirabev®) is being used in combination with cisplatin and paclitaxel as any of the following:
    - as additional treatment for locally advanced unresectable disease clinically positive for residual tumor at the primary site and/or nodes
    - as additional treatment for locally advanced disease with positive margins following resection
    - as primary treatment for metastatic disease beyond the pelvis
    - consider for isolated inguinofemoral/pelvic lymph node recurrence if prior external beam radiation therapy
    - for clinical nodal or distant recurrence with multiple pelvic nodes, distant metastasis, or prior pelvic external beam radiation therapy

Recommended dosage: 15 mg/kg IV every 21 days.

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All indications:

- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), bevacizumab-bvzr (Zirabev®) will be approved through clinical review up to a 12-month duration.

Coverage Limitations[1-3]

Treatment with bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), and bevacizumab-bvzr (Zirabev®) is not considered medically necessary for members with the following concomitant conditions:

- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), and bevacizumab-bvzr (Zirabev®) is not indicated for adjuvant treatment of colon cancer.
- Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), bevacizumab-bvzr (Zirabev®) should not be continued or restarted after disease progression, with the exception of metastatic colorectal cancer.
- Indications not supported by NCCN category 2A or higher recommendations may not be considered medically necessary

Contraindications/Warnings/Precautions[1-3]

Insert contraindications, warnings & precautions from package insert, no need to go into more detail then bullet the main toxicity

- There are no contraindications listed in the US manufacturer's labeling.
- Warnings/precautions:
    - Gastrointestinal perforations/fistula
    - Surgery and wound healing – withhold for at least 28 days prior to elective surgery and do not administer for at least 28 days after surgery and until wound is fully healed
    - Thromboembolism
    - Proteinuria/nephrotic syndrome
    - Hypertension
    - Hemorrhage

For specific recommendations on contraindications, warnings and precautions, patient monitoring, and on dose adjustments and discontinuation, please refer to the current prescribing information.

Billing

- **Description:**
    - Inj., bevacizumab, 10 mg
        - HCPCS: J9035
    - Inj., bevacizumab-awwb, 10 mg

- HCPCS: Q5107
- Inj., bevacizumab-bvzr, 10 mg
  - HCPCS: Q5118

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Drug Coverage Policies are developed as needed, regularly reviewed, updated at least annually, and are subject to change. Other policies and coverage determination guidelines may apply. Federal and state regulatory requirements and member specific benefit plan documents, if applicable, must be reviewed prior to this Drug Coverage Policy. This Drug Coverage Policy is for informational purposes only and does not constitute medical advice or dictate how providers should practice medicine. This policy should not be reproduced, stored in a retrieval system, or altered from its original form without written permission from Oncology Analytics, Inc.

Chemotherapy Regimens

Regimen	Agents
5-FU/LV	Fluorouracil, leucovorin
FOLFOX	Fluorouracil, leucovorin, oxaliplatin
CapeOx	Capecitabine, oxaliplatin
FOLFOXIRI	Fluorouracil, leucovorin, oxaliplatin, irinotecan

References

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3. Zirabev [package insert]. Pfizer Inc., New York, NY. Available at: http://labeling.pfizer.com/ShowLabeling.aspx?id=11860
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