



## Medical Policy Manual **Approved Rev: Do Not Implement until 10/31/25**

### **Bevacizumab Products (Avastin®; Mvasi®; Zirabev™; Alymsys®; Vegzelma™, Avzivi®)**

Some agents on this policy may require step therapy See “Step Therapy Requirements for Provider Administered Specialty Medications” Document at:

[https://www.bcbst.com/docs/providers/Comm\\_BC\\_PAD\\_Step\\_Therapy\\_Guide.pdf](https://www.bcbst.com/docs/providers/Comm_BC_PAD_Step_Therapy_Guide.pdf)

### **IMPORTANT REMINDER**

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

### **POLICY**

### **INDICATIONS**

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

#### FDA-Approved Indications

##### Metastatic Colorectal Cancer (mCRC)

- Avastin, Alymsys, Avzivi, Mvasi, Vegzelma or Zirabev, in combination with intravenous fluorouracil-based chemotherapy, is indicated for the first- or second-line treatment of patients with metastatic colorectal cancer.
- Avastin, Alymsys, Avzivi, Mvasi, Vegzelma or Zirabev, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy, is indicated for the second-line treatment of patients with metastatic colorectal cancer who have progressed on a first-line bevacizumab product-containing regimen.

##### First-Line Non-Squamous Non-Small Cell Lung Cancer (NSCLC)

Avastin, Alymsys, Avzivi, Mvasi, Vegzelma or Zirabev, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer.

##### Recurrent Glioblastoma (RGM)

Avastin, Alymsys, Avzivi, Mvasi, Vegzelma or Zirabev, is indicated for the treatment of recurrent glioblastoma in adults.

##### Metastatic Renal Cell Carcinoma (mRCC)

Avastin, Alymsys, Avzivi, Mvasi, Vegzelma or Zirabev, in combination with interferon alfa, is indicated for the treatment of metastatic renal cell carcinoma.

##### Persistent, Recurrent, or Metastatic Cervical Cancer

Avastin, Alymsys, Avzivi, Mvasi, Vegzelma or Zirabev, in combination with paclitaxel and cisplatin or paclitaxel and topotecan, is indicated for the treatment of patients with persistent, recurrent, or metastatic cervical cancer.

##### Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

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- Avastin, Mvasi, Vegzelma or Zirabev, in combination with carboplatin and paclitaxel, followed by Avastin, Mvasi, Vegzelma or Zirabev as a single agent, is indicated for the treatment of patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection.
- Avastin, Alysmsys, Avzivi, Mvasi, Vegzelma or Zirabev, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan, is indicated for the treatment of patients with platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer who received no more than 2 prior chemotherapy regimens.
- Avastin, Mvasi, Vegzelma or Zirabev, in combination with carboplatin and paclitaxel, or with carboplatin and gemcitabine, followed by Avastin, Mvasi, Vegzelma or Zirabev as a single agent, is indicated for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.

### Hepatocellular Carcinoma

Avastin, in combination with atezolizumab, is indicated for the treatment of patients with unresectable or metastatic hepatocellular carcinoma (HCC) who have not received prior systemic therapy.

### Compendial Uses

- Central Nervous System (CNS) Cancers
  - Circumscribed Glioma
  - Diffuse high grade and high grade gliomas
  - Glioblastoma
  - IDH mutant astrocytoma (WHO Grade 2, 3, or 4)
  - Oligodendroglioma (WHO Grade 2 or 3)
  - Intracranial and Spinal Ependymoma (excluding subependymoma)
  - Medulloblastoma
  - Primary Central Nervous System Lymphoma
  - Meningiomas
  - Limited and Extensive Brain Metastases
  - Metastatic Spine Tumors
  - Primary Spinal Cord Tumors
- Pleural Mesothelioma, Peritoneal Mesothelioma, Pericardial Mesothelioma, Tunica Vaginalis Testis Mesothelioma
- Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer
- Soft Tissue Sarcoma
  - Angiosarcoma
  - Solitary Fibrous Tumor/Hemangiopericytoma
- Uterine Neoplasms/Endometrial Carcinoma
- Vulvar Carcinoma
- Vaginal Cancer
- Cervical Cancer
- Small Bowel Adenocarcinoma
- Ampullary Adenocarcinoma
- Appendiceal Adenocarcinoma
- Anal Adenocarcinoma
- Renal Cell Carcinoma
- Hepatocellular Carcinoma
- Ophthalmic Disorders
  - Diabetic Macular Edema
  - Neovascular (wet) Age-Related Macular Degeneration
  - Macular Edema following Retinal Vein Occlusion



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- Proliferative Diabetic Retinopathy
- Choroidal Neovascularization
- Neovascular Glaucoma
- Retinopathy of Prematurity
- Polypoidal Choroidal Vasculopathy

All other indications are considered experimental/investigational and not medically necessary.

### COVERAGE CRITERIA

#### Ophthalmic Disorders

Authorization of 6 months may be granted for treatment of the following retinal disorders:

- Diabetic Macular Edema
- Neovascular (wet) Age-Related Macular Degeneration
- Macular Edema following Retinal Vein Occlusion
- Proliferative Diabetic Retinopathy
- Choroidal Neovascularization (including myopic choroidal neovascularization, angioid streaks, choroiditis [including choroiditis secondary to ocular histoplasmosis], idiopathic degenerative myopia, retinal dystrophies, rubeosis iridis, pseudoxanthoma elasticum, and trauma)
- Neovascular Glaucoma
- Retinopathy of Prematurity
- Polypoidal Choroidal Vasculopathy

#### Colorectal Cancer (CRC)

Authorization of 12 months may be granted for treatment of colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma.

#### Small Bowel Adenocarcinoma

Authorization of 12 months may be granted for treatment of small bowel adenocarcinoma.

#### Ampullary Adenocarcinoma

Authorization of 12 months may be granted for treatment of intestinal-type ampullary adenocarcinoma that is progressive, unresectable, or metastatic.

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

Authorization of 12 months may be granted for treatment of recurrent, unresectable, advanced, or metastatic non-squamous NSCLC.

#### CNS Cancer

Authorization of 12 months may be granted for treatment of the following types of CNS cancer:

- Circumscribed Glioma
- Diffuse high grade and high grade gliomas
- Glioblastoma
- IDH mutant astrocytoma (WHO Grade 2, 3 or 4)



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- Oligodendroglioma (WHO Grade 2 or 3)
- Intracranial and Spinal Ependymoma (excludes subependymoma)
- Medulloblastoma
- Primary Central Nervous System Lymphoma
- Meningiomas
- Limited and Extensive Brain Metastases
- Metastatic Spine Tumors
- Primary Spinal Cord Tumors

### **Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer**

Authorization of 12 months may be granted for treatment of epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, and malignant sex cord stromal tumors.

### **Uterine Neoplasms/Endometrial Carcinoma**

Authorization of 12 months may be granted for treatment of progressive, persistent, recurrent, or metastatic uterine neoplasms or endometrial carcinoma.

### **Cervical Cancer**

Authorization of 12 months may be granted for treatment of persistent, recurrent, or metastatic cervical cancer.

### **Vaginal Cancer**

Authorization of 12 months may be granted for treatment of recurrent or metastatic vaginal cancer.

### **Renal Cell Carcinoma**

Authorization of 12 months may be granted for treatment of relapsed or stage IV renal cell carcinoma.

### **Soft Tissue Sarcoma**

Authorization of 12 months may be granted for treatment of angiosarcoma, as single agent therapy.

Authorization of 12 months may be granted for treatment of solitary fibrous tumor or hemangiopericytoma, in combination with temozolomide.

### **Mesothelioma**

Authorization of 12 months may be granted for treatment of pleural mesothelioma, peritoneal mesothelioma, pericardial mesothelioma, or tunica vaginalis testis mesothelioma when any of the following criteria are met:

- As first-line therapy in combination with pemetrexed and either cisplatin or carboplatin, followed by single-agent maintenance bevacizumab
- As subsequent therapy in combination with pemetrexed and either cisplatin or carboplatin if immunotherapy was administered as first-line treatment

Authorization of 12 months may be granted for treatment of peritoneal mesothelioma, pericardial mesothelioma, or tunica vaginalis testis mesothelioma when used in combination with atezolizumab as subsequent therapy.



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### Vulvar Carcinoma

Authorization of 12 months may be granted for treatment of advanced, recurrent, or metastatic vulvar carcinoma, including squamous cell carcinoma and adenocarcinoma.

### Hepatocellular Carcinoma

Authorization of 12 months may be granted for treatment of unresectable or extrahepatic/ metastatic hepatocellular carcinoma, when the requested medication will be used as initial treatment in combination with atezolizumab.

Authorization of 12 months may be granted for adjuvant treatment of operable hepatocellular carcinoma, when the member is at a high risk of recurrence and the requested medication will be used in combination with atezolizumab.

### CONTINUATION OF THERAPY

#### Ophthalmic Disorders

For ophthalmic disorders, authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in the coverage criteria section when the member has demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

#### All Other Indications

For all other indications, authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in the coverage criteria section when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

### MEDICATION QUANTITY LIMITS

Drug Name	Diagnosis	Maximum Dosing Regimen
Avastin (Bevacizumab) Alymsys (Bevacizumab-maly) Mvasi (Bevacizumab-awwb) Vegzelma (Bevacizumab-adcd) Zirabev (Bevacizumab-bvzr) Avzivi (Bevacizumab-tnjn)	Ampullary Adenocarcinoma	Route of Administration: Intravenous 5mg/kg every 2 weeks 7.5mg/kg every 3 weeks
Avzivi (Bevacizumab-tnjn)	Ampullary Adenocarcinoma	Route of Administration: Intravenous 5mg/kg every 2 weeks  7.50mg/kg every 3 weeks
Avastin (Bevacizumab) Alymsys (Bevacizumab-maly) Mvasi (Bevacizumab-awwb) Vegzelma (Bevacizumab-adcd) Zirabev (Bevacizumab-bvzr) Avzivi (Bevacizumab-tnjn)	Colorectal Cancer, including Appendiceal Adenocarcinoma and Anal Adenocarcinoma	Route of Administration: Intravenous 10mg/kg every 2 weeks
Avastin (Bevacizumab) Alymsys (Bevacizumab-maly) Mvasi (Bevacizumab-awwb) Vegzelma (Bevacizumab-adcd)	CNS Cancer, including Glioblastoma	Route of Administration: Intravenous 10mg/kg every 2 weeks 15mg/kg every 3 weeks



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Zirabev (Bevacizumab-bvzr) <b>Avzivi (Bevacizumab-tnjn)</b>		
Avastin (Bevacizumab) Alymsys (Bevacizumab-maly) Mvasi (Bevacizumab-awwb) Vegzelma (Bevacizumab-adcd) <b>Zirabev (Bevacizumab-bvzr)</b> <b>Avzivi (Bevacizumab-tnjn)</b>	Cervical Cancer, Hepatocellular Carcinoma, Malignant Pleural Mesothelioma, Malignant Peritoneal Mesothelioma, Pericardial Mesothelioma, or Tunica Vaginalis Testis Mesothelioma, Non-Small Cell Lung Cancer ( <b>NSCLC</b> ), Soft Tissue Sarcoma: Angiosarcoma, Uterine Neoplasms-Endometrial Carcinoma, <b>Vaginal Cancer</b> , Vulvar Carcinoma	Route of Administration: Intravenous 15mg/kg every 3 weeks
Avastin (Bevacizumab) Alymsys (Bevacizumab-maly) Mvasi (Bevacizumab-awwb) Vegzelma (Bevacizumab-adcd) Zirabev (Bevacizumab-bvzr) <b>Avzivi (Bevacizumab-tnjn)</b>	Neovascular Glaucoma (Adjunct), Proliferative Diabetic Retinopathy	Route of Administration: Intravitreal ≥18 Year(s) 1.25mg in the affected eye(s) every 4 weeks
<b>Avastin (Bevacizumab)</b> <b>Alymsys (Bevacizumab-maly)</b> <b>Mvasi (Bevacizumab-awwb)</b> <b>Vegzelma (Bevacizumab-adcd)</b> <b>Zirabev (Bevacizumab-bvzr)</b> <b>Avzivi (Bevacizumab-tnjn)</b>	<b>Diabetic Macular Edema</b>	<b>Route of Administration: Intravitreal</b> <b>≥18 year(s)</b> <b>1.5mg in the affected eye(s) every 4</b> <b>weeks</b>
<b>Avastin (Bevacizumab)</b> <b>Alymsys (Bevacizumab-maly)</b> <b>Mvasi (Bevacizumab-awwb)</b> <b>Vegzelma (Bevacizumab-adcd)</b> <b>Zirabev (Bevacizumab-bvzr)</b> <b>Avzivi (Bevacizumab-tnjn)</b>	Macular Edema following Retinal Vein Occlusion	Route of Administration: Intravitreal ≥18 Year(s) 1.25mg in the affected eye(s) once and repeat at 1 to 3 month intervals
<b>Avastin (Bevacizumab)</b> <b>Alymsys (Bevacizumab-maly)</b> <b>Mvasi (Bevacizumab-awwb)</b> <b>Vegzelma (Bevacizumab-adcd)</b> <b>Zirabev (Bevacizumab-bvzr)</b>	Neovascular (wet) Age- Related Macular Degeneration (AMD), Choroidal Neovascularization	Route of Administration: Intravitreal ≥18 <b>Year(s)</b> 1.25mg in the affected eye(s) every 4 weeks 2.5mg in the affected eye(s) every 4 weeks for 3 doses
<b>Avzivi (Bevacizumab-tnjn)</b>	<b>Neovascular (wet) Age- Related Macular Degeneration (AMD), Choroidal Neovascularization</b>	<b>Route of Administration: Intravitreal</b> <b>≥18 year(s)</b> <b>1.25mg in the affected eye(s) every 4</b> <b>weeks</b>  <b>≥18 year(s)</b> <b>2.50mg in the affected eye(s) every 4</b> <b>weeks for 3 doses</b>
Avastin (Bevacizumab) Alymsys (Bevacizumab-maly)	Ovarian, Fallopian, Primary Peritoneal Cancer	Route of Administration: Intravenous 10mg/kg every 2 weeks



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Mvasi (Bevacizumab-awwb) Vegzelma (Bevacizumab-adcd) Zirabev (Bevacizumab-bvzr) <b>Avzivi (Bevacizumab-tnjn)</b>		15mg/kg every 3 weeks
Avastin (Bevacizumab) Alymsys (Bevacizumab-maly) Mvasi (Bevacizumab-awwb) Vegzelma (Bevacizumab-adcd) Zirabev (Bevacizumab-bvzr) <b>Avzivi (Bevacizumab-tnjn)</b>	Polypoidal Choroidal Vasculopathy	Route of Administration: Intravitreal 2.5mg in the affected eye(s); frequency should not be more frequent than every 4 weeks
Avastin (Bevacizumab) Alymsys (Bevacizumab-maly) Mvasi (Bevacizumab-awwb) Vegzelma (Bevacizumab-adcd) Zirabev (Bevacizumab-bvzr) <b>Avzivi (Bevacizumab-tnjn)</b>	Renal Cell Carcinoma	Route of Administration: Intravenous 10mg/kg every 2 weeks
Avastin (Bevacizumab) Alymsys (Bevacizumab-maly) Mvasi (Bevacizumab-awwb) Vegzelma (Bevacizumab-adcd) Zirabev (Bevacizumab-bvzr) <b>Avzivi (Bevacizumab-tnjn)</b>	Retinopathy of Prematurity	Route of Administration: Intravitreal <18 Year(s) 0.625mg in the affected eye(s) for 1 dose
Avastin (Bevacizumab) Alymsys (Bevacizumab-maly) Mvasi (Bevacizumab-awwb) Vegzelma (Bevacizumab-adcd) Zirabev (Bevacizumab-bvzr) <b>Avzivi (Bevacizumab-tnjn)</b>	Small Bowel Adenocarcinoma	Route of Administration: Intravenous 5mg/kg every 2 weeks 7.5mg/kg every 3 weeks
<b>Avzivi (Bevacizumab-tnjn)</b>	<b>Small Bowel Adenocarcinoma</b>	<b>Route of Administration: Intravenous 5mg/kg every 2 weeks 7.50mg/kg every 3 weeks</b>
Avastin (Bevacizumab) Alymsys (Bevacizumab-maly) Mvasi (Bevacizumab-awwb) Vegzelma (Bevacizumab-adcd) <b>Zirabev (Bevacizumab-bvzr)</b> <b>Avzivi (Bevacizumab-tnjn)</b>	Soft Tissue Sarcoma: Solitary Fibrous Tumor	Route of Administration: Intravenous 5mg/kg every 2 weeks

### APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

### ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex



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Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

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**EFFECTIVE DATE** 10/31/2025

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