

**Clinical Policy: Bevacizumab (Avastin, Mvasi, Zirabev)****Reference Number: LA.PHAR.93****Effective Date:****Last Review Date: 01.21****Line of Business: Medicaid****[Coding](#)  
**[Implications](#)  
**[Revision Log](#)******

**See [Important Reminder](#) at the end of this policy for important regulatory and legal information.**

**Description**

**Bevacizumab (Avastin®), bevacizumab-awwb (Mvasi®), bevacizumab-bvzr (Zirabev™) are vascular endothelial growth factor-specific angiogenesis inhibitors.**

**FDA Approved Indication(s)**

**Avastin, Mvasi, and Zirabev are indicated for the treatment of:**

- **Metastatic colorectal cancer, in combination with intravenous 5-fluorouracil (5-FU)-based chemotherapy for first- or second-line treatment**
- **Metastatic colorectal cancer, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab product-containing regimen**
- **Unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer (NSCLC), in combination with carboplatin and paclitaxel for first-line treatment**
- **Recurrent glioblastoma in adults**
- **Metastatic renal cell carcinoma (RCC) in combination with interferon alfa**
- **Persistent, recurrent, or metastatic cervical cancer, in combination with paclitaxel and cisplatin, or paclitaxel and topotecan**

**Avastin is also indicated for the treatment of:**

- **Epithelial ovarian, fallopian tube, or primary peritoneal cancer:**
  - **In combination with carboplatin and paclitaxel, followed by Avastin as a single agent, for stage III or IV disease following initial surgical resection**
  - **In combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy regimens**
  - **In combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by Avastin as a single agent, for platinum-sensitive recurrent disease**
- **Hepatocellular carcinoma (HCC) in combination with atezolizumab for patients with unresectable or metastatic HCC who have not yet received prior systemic therapy.**

**Limitation(s) of use: Bevacizumab-products are not indicated for adjuvant treatment of colon cancer.**

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#### Policy/Criteria

Prior authorization is required. Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections that Avastin, Mvasi, and Zirabev are medically necessary when the following criteria are met:

#### **I. Initial Approval Criteria**

##### **A. FDA-Approved Indications (must meet all):**

- 1. Diagnosis of one of the following (a-g):**
  - a. Colorectal cancer;**
  - b. Non-squamous non-small cell lung cancer;**
  - c. Glioblastoma;**
  - d. Metastatic renal cell carcinoma;**
  - e. Cervical cancer;**
  - f. Epithelial ovarian, fallopian tube, or primary peritoneal cancer;**
  - g. Hepatocellular carcinoma;**
- 2. Prescribed by or in consultation with an oncologist;**
- 3. Age ≥ 18 years;**
- 4. Member meets one of the following (a-g):**
  - a. For colorectal cancer, used in combination with one of the following (i, ii, iii):**
    - i. 5-FU based chemotherapy;**
    - ii. Irinotecan and oxaliplatin;**
    - iii. Irinotecan if previously received adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months;**
  - b. For non-squamous non-small cell lung cancer, prescribed as one of the following (i-v):**
    - i. Single agent therapy;**
    - ii. In combination with carboplatin and paclitaxel for first line treatment of unresectable, locally advanced, recurrent or metastatic disease;**
    - iii. In combination with pemetrexed;**
    - iv. In combination with Tecentriq®;**
    - v. In combination with erlotinib for sensitizing EGFR mutation-positive histology, recurrent, advanced, or metastatic disease;**
  - c. For glioblastoma, patient has recurrent disease;**
  - d. For metastatic renal cell carcinoma, used as a single-agent or in combination with interferon alfa, everolimus, or erlotinib (for advanced papillary renal cell carcinoma including hereditary leiomyomatosis and renal cell cancer (HLRCC));**
  - e. For cervical cancer, used in combination with paclitaxel and cisplatin, carboplatin, or topotecan for the treatment of persistent, recurrent, or metastatic disease;**

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- f. For epithelial ovarian, fallopian tube, or primary peritoneal cancer, one of the following (i, ii, iii, or iv):
  - i. Prescribed in combination with carboplatin and paclitaxel, followed by bevacizumab as a single agent, for one of the following (1 or 2):
    - 1. Stage III or IV disease following initial surgical resection;
    - 2. Stage II-IV high-grade serous, low-grade serous, endometrioid (Grade 1/2/3), clear cell carcinoma, or carcinosarcoma;
  - ii. For platinum-resistant recurrent disease, prescribed in combination with paclitaxel, pegylated liposomal doxorubicin, topotecan, or cyclophosphamide;
  - iii. For platinum-sensitive recurrent disease, prescribed in combination with carboplatin and paclitaxel, or carboplatin and gemcitabine, or carboplatin and liposomal doxorubicin, followed by bevacizumab as a single agent;
  - iv. Prescribed as a single agent for clinical relapse in patients with stage II-IV malignant sex cord-stromal tumors;
- g. For HCC, used in combination with Tecentriq® as first-line systemic therapy;
- 5. For Avastin requests, member meets one of the following (a or b):
  - a. Medical justification supports inability to use Mvasi or Zirabev (e.g., contraindications to the excipients);\*  
*\*Prior authorization may be required for Mvasi and Zirabev*
  - b. Request is for Stage IV or metastatic cancer or associated conditions. Exception if “clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
- 6. Request meets one of the following (a or b):\*
  - a. Dose does not exceed 15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks (see Appendix F for dose rounding guidelines);
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).  
*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:

Medicaid – 6 months

#### B. Oncology - Non-FDA-Approved Indications (off-label) (must meet all):

- 1. Diagnosis of one of the following conditions (a-m):
  - a. Anaplastic gliomas;
  - b. Breast cancer;
  - c. Endometrial carcinoma;
  - d. Intracranial and spinal ependymoma;
  - e. Low-grade (WHO Grade II) infiltrative supratentorial astrocytoma/oligodendroglioma;
  - f. Malignant pleural mesothelioma;
  - g. Medulloblastoma;
  - h. Meningioma;

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- i. Metastatic spine tumors or brain metastases;
- j. Primary central nervous system cancers;
- k. Small bowel adenocarcinoma;
- l. Soft tissue sarcoma – solitary fibrous tumor or angiosarcoma;
- m. Vulvar cancer – squamous cell carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For Avastin requests, medical justification supports inability to use Mvasi or Zirabev (e.g., contraindications to the excipients);  
*\*Prior authorization may be required*
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).\*  
*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

#### Approval duration:

Medicaid – 6 months

#### C. Ophthalmology - Non-FDA-Approved Indications (off-label) (must meet all):

1. Diagnosis of one of the following conditions (a-g):
  - a. Neovascular (wet) age-related macular degeneration;
  - b. Macular edema following retinal vein occlusion;
  - c. Diabetic macular edema;
  - d. Proliferative diabetic retinopathy;
  - e. Neovascular glaucoma;
  - f. Choroidal neovascularization associated with: angioid streaks, no known cause, inflammatory conditions, high pathologic myopia, or ocular histoplasmosis syndrome;
  - g. Diabetic retinopathy associated with ocular neovascularization (choroidal, retinal, iris);
2. Age ≥ 18 years;
3. Request is for intravitreal Avastin;
4. Request meets one of the following (a or b):
  - a. Dose does not exceed 2.5 mg/dose;
  - b. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

#### Approval duration:

Medicaid – 6 months

#### D. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.

## II. Continued Therapy

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#### A. All Indications in Section I (must meet all):

1. Member meets one of the following (a or b):
  - a. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
  - b. Documentation supports that member is currently receiving Avastin, Mvasi, or Zirabev for a covered oncology indication listed in section I and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Avastin requests for non-ophthalmology uses, member meets one of the following (a or b):
  - a. Medical justification supports inability to use Mvasi or Zirabev (e.g., contraindications to the excipients);\*  
*\*Prior authorization may be required for Mvasi and Zirabev*
  - b. Request is for Stage IV or metastatic cancer or associated conditions. Exception if “clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
4. If request is for a dose increase, request meets one of the following (a or b):\*
  - a. New dose does not exceed 15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks (see Appendix F for dose rounding guidelines);
  - b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).  
*\*Prescribed chemotherapy regimen must be FDA-approved or recommended by NCCN*

#### Approval duration:

Medicaid – 6 months

#### B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Louisiana Healthcare Connections benefit and documentation supports positive response to therapy.  
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.

### III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy –LA.PMN.53 for Medicaid, or evidence of coverage documents.

### IV. Appendices/General Information

#### Appendix A: Abbreviation/Acronym Key

5-FU: fluorouracil

FDA: Food and Drug Administration

FOLFIRI: fluorouracil, leucovorin, irinotecan

FOLFOX: fluorouracil, leucovorin, oxaliplatin

HCC: hepatocellular carcinoma

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**HLRCC: hereditary leiomyomatosis  
and renal cell cancer**

**NCCN: National Comprehensive  
Cancer Network**

### **Appendix B: Therapeutic Alternatives**

**This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may require prior authorization.**

<b><u>Drug Name</u></b>	<b><u>Dosing Regimen</u></b>	<b><u>Dose Limit/ Maximum Dose</u></b>
<b><u>Metastatic carcinoma of the colon or rectum</u></b>		
<b><u>FOLFOX4 = Infusional 5-FU/leucovorin/ oxaliplatin</u></b>	<b><u>Oxaliplatin 85 mg/m<sup>2</sup> IV over 2 hours day 1; leucovorin 200 mg/m<sup>2</sup> IV over 2 hours days 1 &amp; 2, followed by 5-FU 400 mg/m<sup>2</sup> IV bolus over 2-4 minutes, followed by 600 mg/m<sup>2</sup> IV 5-FU continuous infusion over 22 hours on days 1 &amp; 2. Repeat cycle every 14 days.</u></b>	<b><u>Varies</u></b>
<b><u>FOLFIRI = Infusional 5-FU/ leucovorin/Camptosar<sup>®</sup> (irinotecan)</u></b>	<b><u>Camptosar 180 mg/m<sup>2</sup> IV over 90 minutes day 1; Leucovorin 400 mg/m<sup>2</sup> IV over 2 hours day 1 followed by 5-FU 400 mg/m<sup>2</sup> IV bolus over 2-4 minutes, followed by 2.4 gm/m<sup>2</sup> IV 5-FU continuous infusion over 46 hours. Repeat cycle every 14 days.</u></b>	<b><u>Varies</u></b>
<b><u>capecitabine (Xeloda<sup>®</sup>)</u></b>	<b><u>2500 mg/m<sup>2</sup> PO BID for 2 weeks; repeat cycles of 2 weeks on and 1 week off. For patients who cannot tolerate intensive therapy.</u></b>	<b><u>Varies</u></b>
<b><u>IROX = oxaliplatin/ Camptosar (irinotecan)</u></b>	<b><u>Oxaliplatin 85 mg/m<sup>2</sup> IV followed by Camptosar 200 mg m<sup>2</sup> IV over 30-90 minutes every 3 weeks</u></b>	<b><u>Varies</u></b>
<b><u>Camptosar (irinotecan)</u></b>	<b><u>180 mg/m<sup>2</sup> IV every 2 weeks or 300-350 mg/m<sup>2</sup> IV every 3 weeks</u></b>	<b><u>Varies</u></b>
<b><u>NSCLC</u></b>		
<b><u>cisplatin carboplati n paclitaxel docetaxel vinorelbine gemcitabin e etoposide</u></b>	<b><u>Various doses</u></b>	<b><u>Varies</u></b>

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<u>Drug Name</u>	<u>Dosing Regimen</u>	<u>Dose Limit/ Maximum Dose</u>
<u>irinotecan</u> <u>vinblastine</u> <u>mitomycin</u> <u>ifosfamide</u> <u>pemetrexed</u> <u>disodium (Alimta®)</u> <u>(2<sup>nd</sup> line)</u> <u>erlotinib (Tarceva®)</u> <u>Tecentrig®</u> <u>(atezolizumab)</u>		
<i><u>Ovarian Cancer</u></i>		
<u>carboplatin and paclitaxel</u>	<u>Carboplatin dosed at an area under the curve (AUC) of 5-7.5 and paclitaxel 175 mg/m<sup>2</sup> IV over 3 hours given every 3 weeks for 6 courses.</u>	<u>Varies</u>
<u>docetaxel taxotere and carboplatin</u>	<u>Docetaxel, 60-75 mg/m<sup>2</sup> IV over 1 hour plus carboplatin dosed at AUC of 5 to 6 every 3 weeks.</u>	<u>Varies</u>
<i><u>Glioblastoma Multiforme</u></i>		
<u>temozolomide (Temodar®)</u>	<u>Maintenance phase cycles: 150 mg-200 mg/m<sup>2</sup> PO days 1-5. Repeat every 28 days.</u>	<u>Varies</u>
<u>carmustine (Bicnu®)</u>	<u>150 mg to 200 mg/m<sup>2</sup> IV on day 1. Repeat every 6-8 weeks for one year or tumor progression.</u>	<u>Varies</u>
<i><u>Cervical Cancer</u></i>		
<u>cisplatin/paclitaxel</u>	<u>Paclitaxel: 135 mg/m<sup>2</sup> IV as a continuous infusion over 24 hours day 1</u>  <u>Cisplatin: 50 mg/m<sup>2</sup> IV on day 2</u>  <u>Repeat cycle every 21 days for up to a total of 6 cycles; responders may continue beyond 6 cycles</u>	<u>Varies</u>
<u>carboplatin/paclitaxel</u>	<u>Paclitaxel: 175 mg/m<sup>2</sup> IV followed by carboplatin AUC 5-6 IV</u>  <u>Repeat every 21 days for up to 6 cycles</u>	<u>Varies</u>
<u>cisplatin/topotecan</u>	<u>Topotecan: 10.75 mg/m<sup>2</sup>/day IV on</u>	<u>Varies</u>



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<u>Drug Name</u>	<u>Dosing Regimen</u>	<u>Dose Limit/ Maximum Dose</u>
<u>(Hycamtin®)</u>	<u>days 1, 2, and 3</u>  <u>Cisplatin: 50 mg/m<sup>2</sup> IV on day 1 only</u>  <u>Repeat cycle every 21 days for up to a total of 6 cycles; responders may continue beyond 6 cycles</u>	
<u>topotecan (Hycamtin®)/paclitaxel</u>	<u>Paclitaxel: 135 mg/m<sup>2</sup> IV continuous infusion over 24 hours day 1</u>  <u>Topotecan: 0.75 mg/m<sup>2</sup>/day IV on days 1, 2, and 3</u>  <u>Repeat cycle every 21 days for up to a total of 6 cycles; responders may continue beyond 6 cycles</u>	<u>Varies</u>

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

### Appendix C: Contraindications/Boxed Warnings

None reported

### Appendix D: General Information

- The FDA revoked the approval of the breast cancer indication for Avastin (bevacizumab) on November 18, 2011. Avastin used for metastatic breast cancer has not been shown to provide a benefit, in terms of delay in the growth of tumors that would justify its serious and potentially life-threatening risks. Nor is there evidence that use of Avastin will either help women with breast cancer live longer or improve their quality of life. More information at: <http://www.fda.gov/NewsEvents/Newsroom/ucm279485.htm>
- Fatal pulmonary hemorrhage can occur in patients with NSCLC treated with chemotherapy and bevacizumab. The incidence of severe or fatal hemoptysis was 31% in patients with squamous histology and 2.3% with NSCLC excluding predominant squamous histology. Patients with recent hemoptysis should not receive bevacizumab.

### Appendix F: Dose Rounding Guidelines

<u>Weight-based Dose Range</u>	<u>Vial Quantity Recommendation</u>
<u>&lt; 104.99 mg</u>	<u>1 vial of 100 mg/4 mL</u>
<u>105 mg-209.99 mg</u>	<u>2 vials of 100 mg/4 mL</u>



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<u>Weight-based Dose Range</u>	<u>Vial Quantity Recommendation</u>
<u>210 mg-314.99 mg</u>	<u>3 vials of 100 mg/4 mL</u>
<u>315 mg-419.99 mg</u>	<u>1 vial of 400 mg/16 mL</u>
<u>420 mg-524.99 mg</u>	<u>1 vial of 100 mg/4 mL and 1 vial of 400 mg/16 mL</u>
<u>525 mg-629.99 mg</u>	<u>2 vials of 100 mg/4 mL and 1 vial of 400 mg/16 mL</u>
<u>630 mg-734.99 mg</u>	<u>3 vials of 100 mg/4 mL and 1 vial of 400 mg/16 mL</u>
<u>735 mg-839.99 mg</u>	<u>2 vials of 400 mg/16 mL</u>
<u>881 mg-944.99 mg</u>	<u>1 vials of 100 mg/4 mL and 2 vials of 400 mg/16 mL</u>
<u>945 mg-1,049.99 mg</u>	<u>2 vials of 100 mg/4 mL and 2 vials of 400 mg/16 mL</u>
<u>1,050 mg-1,154.99 mg</u>	<u>3 vials of 100 mg/4 mL and 2 vials of 400 mg/16 mL</u>
<u>1,155 mg-1,259.99 mg</u>	<u>3 vials of 400 mg/16 mL</u>
<u>1,260 mg-1,364.99 mg</u>	<u>1 vials of 100 mg/4 mL and 3 vials of 400 mg/16 mL</u>
<u>1,365 mg-1,469.99 mg</u>	<u>2 vials of 100 mg/4 mL and 3 vials of 400 mg/16 mL</u>
<u>1,470 mg-1,574.99 mg</u>	<u>3 vials of 100 mg/4 mL and 3 vials of 400 mg/16 mL</u>
<u>1,575 mg-1,679.99 mg</u>	<u>4 vials of 400 mg/16 mL</u>
<u>1,680 mg-1,784.99 mg</u>	<u>1 vials of 100 mg/4 mL and 4 vials of 400 mg/16 mL</u>
<u>1,785 mg-1,889.99 mg</u>	<u>2 vials of 100 mg/4 mL and 4 vials of 400 mg/16 mL</u>
<u>1,890 mg-1,994.99 mg</u>	<u>3 vials of 100 mg/4 mL and 4 vials of 400 mg/16 mL</u>
<u>1,995 mg-2,099.99 mg</u>	<u>5 vials of 400 mg/16 mL</u>

### V. Dosage and Administration

<u>Indication</u>	<u>Dosing Regimen</u>	<u>Maximum Dose</u>
<u>Metastatic colorectal cancer</u>	<u>5 mg/kg or 10 mg/kg once every 14 days as an IV infusion in combination with a 5-FU based chemotherapy regimen until disease progression is detected. 5 mg/kg every 2 weeks or 7.5 mg/kg every 3 weeks when used in combination with a fluoropyrimidine-irinotecan or fluoropyrimidine-oxaliplatin based chemotherapy regimen in patients who have progressed on a first-line Avastin-containing regimen</u>	<u>15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks</u>
<u>Non-squamous, non-small cell lung cancer</u>	<u>15 mg/kg IV infusion every 3 weeks with carboplatin/paclitaxel</u>	<u>15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks</u>

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<u>Indication</u>	<u>Dosing Regimen</u>	<u>Maximum Dose</u>
<u>Ovarian cancer</u>	<u>15 mg/kg IV infusion every 3 weeks</u>	<u>15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks</u>
<u>Platinum resistant ovarian cancer</u>	<u>10 mg/kg intravenously every 2 weeks with weekly paclitaxel, liposomal doxorubicin, or</u>	<u>15 mg/kg IV every 3 weeks or 10 mg/kg</u>
<u>HCC</u>	<u>15 mg/kg IV every 3 weeks plus Tecentriq 1,200 mg IV on the same day</u>	<u>15 mg/kg IV every 3 weeks</u>
<u>Clear cell renal carcinoma</u>	<u>10 mg/kg IV every 2 weeks with interferon alfa</u>	<u>15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks</u>
<u>Glioblastoma multiforme, anaplastic astrocytoma, anaplastic oligodendroglioma</u>	<u>10 mg/kg IV every 2 weeks</u>	<u>15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks</u>
<u>Soft tissue sarcoma</u>	<u>15 mg/kg IV infusion every 3 weeks</u>	<u>15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks</u>
<u>Cervical cancer</u>	<u>15 mg/kg IV infusion every 3 weeks (in combination with paclitaxel and either cisplatin or topotecan) until</u>	<u>15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks</u>
<u>Neovascular (wet) macular degeneration</u>	<u>1.25 to 2.5 mg administered by intravitreal injection every 4 weeks</u>	<u>2.5 mg/dose</u>
<u>Neovascular glaucoma</u>	<u>1.25 mg administered by intravitreal injection every 4 weeks</u>	<u>2.5 mg/dose</u>
<u>Macular edema secondary to retinal vein occlusion</u>	<u>1 mg to 2.5 mg administered by intravitreal injection every 4 weeks</u>	<u>2.5 mg/dose</u>
<u>Proliferative diabetic retinopathy</u>	<u>1.25 mg administer by intravitreal injection 5 to 20 days before vitrectomy</u>	<u>2.5 mg/dose</u>
<u>Diabetic macular edema</u>	<u>1.25 mg administered by intravitreal injection</u>	<u>2.5 mg/dose</u>

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<u>Indication</u>	<u>Dosing Regimen</u>	<u>Maximum Dose</u>
<u>Malignant mesothelioma of pleura</u>	<u>15 mg/kg IV (plus pemetrexed 500 mg/m(2) IV and cisplatin 75 mg/m(2) IV) every 21 days for up to 6 cycles, followed by maintenance bevacizumab 15 mg/kg every 21 days until disease progression or unacceptable toxicity. All patients should receive folic acid 400 mcg orally daily and vitamin B12 1000 mcg IM every 3 weeks, both beginning 7 days prior to pemetrexed and continuing for 3 weeks following the last pemetrexed dose (off-label dosage).</u>	<u>2.5 mg/dose</u>
<u>Metastatic colorectal cancer in previously untreated elderly patients ineligible for oxaliplatin- or irinotecan-based chemotherapy</u>	<u>7.5 mg/kg IV on day 1 with capecitabine 1,000 mg/m2 orally twice daily on days 1 to 14, given every 3 weeks until disease progression.</u>	<u>15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2</u>

### VI. Product Availability

Single-use vials: 100 mg/4 mL, 400 mg/16 mL

### VII. References

1. Avastin Prescribing Information. South San Francisco, CA: Genentech, Inc. May 2020. Available at: [www.avastin.com](http://www.avastin.com). Accessed July 6, 2020.
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3. Zirabev Prescribing Information. New York, NY: Pfizer Inc. June 2019. Available at: <http://labeling.pfizer.com/ShowLabeling.aspx?id=11860>. Accessed July 6, 2020.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed July 6, 2020.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: <http://www.clinicalpharmacology-ip.com/>.
6. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; September 2019. Available at: [www.aao.org/ppp](http://www.aao.org/ppp). Accessed July 6, 2020.
7. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Retinal Vein Occlusions. San Francisco, CA: American Academy of Ophthalmology; September 2019. Available at: [www.aao.org/ppp](http://www.aao.org/ppp). Accessed July 6, 2020.

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8. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Diabetic Retinopathy. San Francisco, CA: American Academy of Ophthalmology; September 2019. Available at: [www.aao.org/ppp](http://www.aao.org/ppp). Accessed July 6, 2020.

#### Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

<u>HCPCS Codes</u>	<u>Description</u>
<u>J9035</u>	<u>Injection, bevacizumab, 10 mg</u>
<u>C9257</u>	<u>Injection, bevacizumab, 0.25 mg</u>
<u>Q5107</u>	<u>Injection, bevacizumab-awwb, biosimilar, (Mvasi), 10 mg</u>
<u>Q5118</u>	<u>Injection, bevacizumab-bvcr, biosimilar, (Zirabev), 10 mg</u>

#### ICD-10-CM Diagnosis Codes that Support Coverage Criteria

The following is a list of diagnosis codes that support coverage for the applicable covered procedure code(s).

<u>ICD-10-CM Code</u>	<u>Description</u>
<u>A18.53</u>	<u>Tuberculosis chorioretinitis</u>
<u>C17.0 – C17.9</u>	<u>Malignant neoplasm of small intestine</u>
<u>C18.0 – C18.9</u>	<u>Malignant neoplasm of colon</u>
<u>C19</u>	<u>Malignant neoplasm of rectosigmoid junction</u>
<u>C20</u>	<u>Malignant neoplasm of rectum</u>
<u>C21.8</u>	<u>Malignant neoplasm of overlapping sites of rectum, anus and anal canal</u>
<u>C33</u>	<u>Malignant neoplasm of trachea</u>
<u>C34.00 – C34.02</u>	<u>Malignant neoplasm of main bronchus</u>
<u>C34.10 – C34.12</u>	<u>Malignant neoplasm of upper lobe, bronchus or lung</u>
<u>C34.2</u>	<u>Malignant neoplasm of middle lobe, bronchus or lung</u>
<u>C34.30 – C34.32</u>	<u>Malignant neoplasm of lower lobe, bronchus or lung</u>
<u>C34.80 – C34.82</u>	<u>Malignant neoplasm of overlapping sites of bronchus and lung</u>
<u>C34.90 – C34.92</u>	<u>Malignant neoplasm of unspecified part of bronchus or lung</u>
<u>C48.0 – C48.8</u>	<u>Malignant neoplasm of retroperitoneum and peritoneum</u>
<u>C49.0 – C49.9</u>	<u>Malignant neoplasm of other connective and soft tissue</u>
<u>C50.01 – C50.929</u>	<u>Malignant neoplasm of breast</u>
<u>C53.0 – C53.9</u>	<u>Malignant neoplasm of cervix uteri</u>
<u>C54.0 – C55</u>	<u>Malignant neoplasm of corpus uteri</u>
<u>C56.1 – C56.9</u>	<u>Malignant neoplasm of ovary</u>
<u>C57.0 – C57.9</u>	<u>Malignant neoplasm of other and unspecified female genital organs</u>
<u>C64.1 – C64.9</u>	<u>Malignant neoplasm of kidney, except renal pelvis</u>

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Bevacizumab, Bevacizumab-awwb, Bevacizumab-bvzr

<u>ICD-10-CM Code</u>	<u>Description</u>
<u>C65.1 – C65.9</u>	<u>Malignant neoplasm of renal pelvis</u>
<u>C70.0 – C70.9</u>	<u>Malignant neoplasm of meninges</u>
<u>C71.0 – C71.9</u>	<u>Malignant neoplasm of brain</u>
<u>C72.0 – C72.9</u>	<u>Malignant of spinal cord, cranial neoplasm nerves and other parts of central nervous system</u>
<u>D32.0 – D32.9</u>	<u>Benign neoplasm of meninges</u>
<u>D42.0 – D42.9</u>	<u>Neoplasm of uncertain behavior of meninges</u>
<u>E08.311,</u> <u>E08.3211 – E08.3219,</u> <u>E08.3311 – E08.3319,</u> <u>E08.3411 – E08.3419,</u> <u>E08.3511 – E08.3519</u>	<u>Diabetes mellitus due to underlying condition with diabetic retinopathy with macular edema</u>
<u>E09.311,</u> <u>E09.3211 – E09.3219,</u> <u>E09.3311 – E09.3319,</u> <u>E09.3411 – E09.3419,</u> <u>E09.3511 – E09.3519</u>	<u>Drug or chemical induced diabetes mellitus with diabetic retinopathy with macular edema</u>
<u>E10.311,</u> <u>E10.3211 – E10.3219,</u> <u>E10.3311 – E10.3319,</u> <u>E10.3411 – E10.3419,</u> <u>E10.3511 – E10.3519</u>	<u>Type 1 diabetes mellitus with diabetic retinopathy with macular edema</u>
<u>E11.311,</u> <u>E11.3211 – E11.3219,</u> <u>E11.3311 – E11.3319,</u> <u>E11.3411 – E11.3419,</u> <u>E11.3511 – E11.3519</u>	<u>Type 2 diabetes mellitus with diabetic retinopathy with macular edema</u>
<u>E13.311,</u> <u>E13.3211 – E13.3219,</u> <u>E13.3311 – E13.3319,</u> <u>E13.3411 – E13.3419,</u> <u>E13.3511 – E13.3519</u>	<u>Other specified diabetes mellitus with diabetic retinopathy with macular edema</u>
<u>H16.401 – H16.449</u>	<u>Corneal neovascularization</u>
<u>H30.001 – H30.049</u>	<u>Focal chorioretinal inflammation</u>
<u>H30.101 – H30.139</u>	<u>Disseminated chorioretinal inflammation</u>
<u>H30.891 – H30.899</u>	<u>Other chorioretinal inflammations</u>
<u>H30.90 – H30.93</u>	<u>Unspecified chorioretinal inflammations</u>
<u>H32</u>	<u>Chorioretinal disorders in diseases classified elsewhere</u>
<u>H34.8110 – H 34.8192</u>	<u>Central retinal vein occlusion</u>
<u>H34.8310 – H34.8392</u>	<u>Tributary (branch) retinal vein occlusion</u>
<u>H35.051 – H35.059</u>	<u>Retinal neovascularization, unspecified</u>
<u>H35.141 – H35.169</u>	<u>Retinopathy of prematurity, stages 3 through 5</u>
<u>H35.3210 – H35.3293</u>	<u>Exudative age-related macular degeneration</u>

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<u>ICD-10-CM Code</u>	<u>Description</u>
<u>H35.33</u>	<u>Angioid streaks of macula</u>
<u>H35.81</u>	<u>Retinal edema</u>
<u>H40.50X0-H40.53X4</u>	<u>Glaucoma secondary to other eye disorders [associated with vascular disorders of eye]</u>
<u>H44.20-H44.23</u>	<u>Degenerative myopia</u>
<u>H44.2A1-H44.2A9</u>	<u>Degenerative myopia with choroidal neovascularization</u>
<u>I67.89</u>	<u>Other cerebrovascular disease</u>
<u>Z85.038</u>	<u>Personal history of other malignant neoplasm of large intestine</u>
<u>Z85.048</u>	<u>Personal history of other malignant neoplasm of rectum, rectosigmoid junction, and anus</u>
<u>Z85.068</u>	<u>Personal history of other malignant neoplasm of small intestine</u>
<u>Z85.118</u>	<u>Personal history of other malignant neoplasm of bronchus and</u>
<u>Z85.3</u>	<u>Personal history of malignant neoplasm of breast</u>
<u>Z85.41</u>	<u>Personal history of malignant neoplasm of cervix uteri</u>
<u>Z85.42</u>	<u>Personal history of malignant neoplasm of other parts of uterus</u>
<u>Z85.43</u>	<u>Personal history of malignant neoplasm of ovary</u>
<u>Z85.44</u>	<u>Personal history of malignant neoplasm of other female genital organs</u>
<u>Z85.528</u>	<u>Personal history of other malignant neoplasm of kidney</u>
<u>Z85.53</u>	<u>Personal history of malignant neoplasm of renal pelvis</u>
<u>Z85.841</u>	<u>Personal history of malignant neoplasm of brain</u>
<u>Z85.848</u>	<u>Personal history of malignant neoplasm of other parts of nervous tissue</u>

[illegible]

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### Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

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