

## **Clinical Policy: Bevacizumab (Avastin, Mvasi, Zirabev)**

Reference Number: CP.PHAR.93

Effective Date: 12.01.11

Last Review Date: 05.20

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)

[Revision Log](#)

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

### **Description**

Bevacizumab (Avastin<sup>®</sup>), bevacizumab-awwb (Mvasi<sup>®</sup>), bevacizumab-bvzr (Zirabev<sup>™</sup>) 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

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

### **Policy/Criteria**

*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 health plans affiliated with Centene Corporation<sup>®</sup> 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-f):
  - a. Colorectal cancer;
  - b. Non-squamous non-small cell lung cancer;
  - c. Glioblastoma;
  - d. Metastatic renal cell carcinoma;
  - e. Carcinoma of the cervix;
  - f. Epithelial ovarian, fallopian tube, or primary peritoneal cancer;
2. Member meets one of the following (a-f):
  - a. For colorectal cancer, used in combination with 5-FU based chemotherapy;
  - b. For non-squamous non-small cell lung cancer, use in combination with carboplatin and paclitaxel for first line treatment of unresectable, locally advanced, recurrent or metastatic disease;
  - c. For glioblastoma, patient has recurrent disease;
  - d. For metastatic renal cell carcinoma, used in combination with interferon alfa;
  - e. For cervical cancer, used in combination with paclitaxel and cisplatin or topotecan for the treatment of persistent, recurrent, or metastatic disease;
  - f. For epithelial ovarian, fallopian tube, or primary peritoneal cancer, one of the following (i, ii, or iii):
    - i. In combination with carboplatin and paclitaxel, followed by bevacizumab as a single agent, for stage III or IV disease following initial surgical resection;
    - ii. In combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy regimens;
    - iii. In combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by bevacizumab as a single agent, for platinum-sensitive recurrent disease;
3. Prescribed by or in consultation with an oncologist;
4. Age  $\geq$  18 years;
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 for a State with regulations against step therapy in advanced oncology settings (*see Appendix E*);
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;
  - 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/HIM** – 6 months

**Commercial** – Length of Benefit

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

1. Diagnosis of one of the following conditions (a-l):
  - a. AIDs-related Kaposi sarcoma;
  - b. Anaplastic gliomas;
  - c. Breast cancer;
  - d. Endometrial carcinoma;
  - e. Intracranial and spinal ependymoma;
  - f. Low-grade (WHO Grade II) infiltrative supratentorial astrocytoma/oligodendroglioma;
  - g. Malignant pleural mesothelioma;
  - h. Medulloblastoma;
  - i. Meningioma;
  - j. Primary central nervous system cancers;
  - k. Small bowel adenocarcinoma;
  - l. Soft tissue sarcoma;
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/HIM** – 6 months**Commercial** – Length of Benefit**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 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/HIM** – 6 months

**Commercial** – Length of Benefit

**D. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

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

1. Member meets one of the following (a or b):
  - a. Currently receiving medication via Centene 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 for a State with regulations against step therapy in advanced oncology settings (*see Appendix E*);
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;
  - 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/HIM** – 6 months

**Commercial** – Length of Benefit

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

1. Currently receiving medication via Centene 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 for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.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 policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.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

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 not be a formulary agent for all relevant lines of business and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<b><i>Metastatic carcinoma of the colon or rectum</i></b>		
FOLFOX4 = Infusional 5-FU/leucovorin/ oxaliplatin	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 & 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 & 2. Repeat cycle every 14 days.	Varies
FOLFIRI = Infusional 5-FU/ leucovorin/Camptosar <sup>∇</sup> (irinotecan)	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.	Varies
capecitabine (Xeloda <sup>∇</sup> )	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.	Varies
<b><i>NSCLC</i></b>		
cisplatin carboplatin paclitaxel docetaxel	Various doses	Varies

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
vinorelbine gemcitabine etoposide irinotecan vinblastine mitomycin ifosfamide pemetrexed disodium (Alimta®) (2 <sup>nd</sup> line)		
<b><i>Ovarian Cancer</i></b>		
carboplatin and paclitaxel	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.	Varies
docetaxel taxotere and carboplatin	Docetaxel, 60-75 mg/m <sup>2</sup> IV over 1 hour plus carboplatin dosed at AUC of 5 to 6 every 3 weeks.	Varies
<b><i>Glioblastoma Multiforme</i></b>		
temozolomide (Temodar®)	Maintenance phase cycles: 150 mg-200 mg/m <sup>2</sup> PO days 1-5. Repeat every 28 days.	Varies
<b><i>Cervical Cancer</i></b>		
cisplatin/paclitaxel	Paclitaxel: 135 mg/m <sup>2</sup> IV as a continuous infusion over 24 hours day 1  Cisplatin: 50 mg/m <sup>2</sup> IV on day 2  Repeat cycle every 21 days for up to a total of 6 cycles; responders may continue beyond 6 cycles	Varies
cisplatin/topotecan (Hycamtin®)	Topotecan: 10.75 mg/m <sup>2</sup> /day IV on days 1, 2, and 3  Cisplatin: 50 mg/m <sup>2</sup> IV on day 1 only  Repeat cycle every 21 days for up to a total of 6 cycles; responders may continue beyond 6 cycles	Varies
topotecan (Hycamtin®)/paclitaxel	Paclitaxel: 135 mg/m <sup>2</sup> IV continuous infusion over 24 hours day 1  Topotecan: 0.75 mg/m <sup>2</sup> /day IV on days 1, 2, and 3	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Repeat cycle every 21 days for up to a total of 6 cycles; responders may continue beyond 6 cycles	

*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 E. States with Regulations against Redirections in Stage IV or Metastatic Cancer*

State	Step Therapy Prohibited?	Notes
AR	Yes	For metastatic cancer, <b>unless</b> the preferred drug is consistent with “best practices” (1) used for treatment under (A) FDA-approved indication, or (B) National Comprehensive Cancer Network Drugs & Biologics Compendium; or (2) using evidence-based, peer-reviewed, recognized medical literature. Note – may not require step therapy a second time for same Rx drug.
FL	Yes	For stage 4 metastatic cancer and associated conditions.
GA	Yes	For stage 4 metastatic cancer
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA.
LA	Yes	For stage 4 advanced, metastatic cancer or associated conditions. Exception if “clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes	For advanced metastatic cancer and associated conditions
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

## V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Metastatic colorectal cancer	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	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks
Non-squamous, non-small	15 mg/kg IV infusion every 3 weeks with carboplatin/paclitaxel	15 mg/kg IV every 3 weeks or 10 mg/kg
Ovarian cancer	15 mg/kg IV infusion every 3 weeks	15 mg/kg IV every 3 weeks or 10 mg/kg
Platinum resistant	10 mg/kg intravenously every 2 weeks with weekly paclitaxel, liposomal doxorubicin, or topotecan	15 mg/kg IV every 3 weeks or 10 mg/kg

## 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. June 2019. Available at: [www.avastin.com](http://www.avastin.com). Accessed August 9, 2019.
2. Mvasi Prescribing Information. Thousand Oaks, CA: Amgen Inc. June 2019. Available at: <https://www.mvasi.com/hcp>. Accessed August 9, 2019.
3. Zirabev Prescribing Information. New York, NY: Pfizer Inc. June 2019. Available at: <http://labeling.pfizer.com/ShowLabeling.aspx?id=11860>. Accessed August 9, 2019.
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 September 30, 2019.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: <http://www.clinicalpharmacology-ip.com/>.
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7. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Retinal Vein Occlusions. San Francisco, CA: American Academy of Ophthalmology; November 2015. Available at: [www.aao.org/ppp](http://www.aao.org/ppp). Accessed August 9, 2019.
8. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Diabetic Retinopathy. San Francisco, CA: American Academy of Ophthalmology; December 2017. Available at: [www.aao.org/ppp](http://www.aao.org/ppp). Accessed August 9, 2019.



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#### 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.

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

#### 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).

ICD-10-CM Code	Description
A18.53	Tuberculosis chorioretinitis
C17.0 – C17.9	Malignant neoplasm of small intestine
C18.0 – C18.9	Malignant neoplasm of colon
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C33	Malignant neoplasm of trachea
C34.00 – C34.02	Malignant neoplasm of main bronchus
C34.10 – C34.12	Malignant neoplasm of upper lobe, bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30 – C34.32	Malignant neoplasm of lower lobe, bronchus or lung
C34.80 – C34.82	Malignant neoplasm of overlapping sites of bronchus and lung
C34.90 – C34.92	Malignant neoplasm of unspecified part of bronchus or lung
C46.0-C46.9	Kaposi's sarcoma
C48.0 – C48.8	Malignant neoplasm of retroperitoneum and peritoneum
C49.0 – C49.9	Malignant neoplasm of other connective and soft tissue
C50.01 – C50.929	Malignant neoplasm of breast
C53.0 – C53.9	Malignant neoplasm of cervix uteri
C54.0 – C55	Malignant neoplasm of corpus uteri
C56.1 – C56.9	Malignant neoplasm of ovary
C57.0 – C57.9	Malignant neoplasm of other and unspecified female genital organs
C64.1 – C64.9	Malignant neoplasm of kidney, except renal pelvis
C65.1 – C65.9	Malignant neoplasm of renal pelvis
C70.0 – C70.9	Malignant neoplasm of meninges
C71.0 – C71.9	Malignant neoplasm of brain
C72.0 – C72.9	Malignant of spinal cord, cranial neoplasm nerves and other parts of central nervous system
D32.0 – D32.9	Benign neoplasm of meninges

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ICD-10-CM Code	Description
D42.0 – D42.9	Neoplasm of uncertain behavior of meninges
E08.311, E08.3211 – E08.3219, E08.3311 – E08.3319, E08.3411 – E08.3419, E08.3511 – E08.3519	Diabetes mellitus due to underlying condition with diabetic retinopathy with macular edema
E09.311, E09.3211 – E09.3219, E09.3311 – E09.3319, E09.3411 – E09.3419, E09.3511 – E09.3519	Drug or chemical induced diabetes mellitus with diabetic retinopathy with macular edema
E10.311, E10.3211 – E10.3219, E10.3311 – E10.3319, E10.3411 – E10.3419, E10.3511 – E10.3519	Type 1 diabetes mellitus with diabetic retinopathy with macular edema
E11.311, E11.3211 – E11.3219, E11.3311 – E11.3319, E11.3411 – E11.3419, E11.3511 – E11.3519	Type 2 diabetes mellitus with diabetic retinopathy with macular edema
E13.311, E13.3211 – E13.3219, E13.3311 – E13.3319, E13.3411 – E13.3419, E13.3511 – E13.3519	Other specified diabetes mellitus with diabetic retinopathy with macular edema
H16.401 – H16.449	Corneal neovascularization
H30.001 – H30.049	Focal chorioretinal inflammation
H30.101 – H30.139	Disseminated chorioretinal inflammation
H30.891 – H30.899	Other chorioretinal inflammations
H30.90 – H30.93	Unspecified chorioretinal inflammations
H32	Chorioretinal disorders in diseases classified elsewhere
H34.8110 – H 34.8192	Central retinal vein occlusion
H34.8310 – H34.8392	Tributary (branch) retinal vein occlusion
H35.051 – H35.059	Retinal neovascularization, unspecified
H35.141 – H35.169	Retinopathy of prematurity, stages 3 through 5
H35.3210 – H35.3293	Exudative age-related macular degeneration
H35.33	Angioid streaks of macula
H35.81	Retinal edema
H40.50X0-H40.53X4	Glaucoma secondary to other eye disorders [associated with vascular disorders of eye]
H44.20-H44.23	Degenerative myopia
H44.2A1-H44.2A9	Degenerative myopia with choroidal neovascularization
I67.89	Other cerebrovascular disease

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ICD-10-CM Code	Description
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.048	Personal history of other malignant neoplasm of rectum, rectosigmoid junction, and anus
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.3	Personal history of malignant neoplasm of breast
Z85.41	Personal history of malignant neoplasm of cervix uteri
Z85.42	Personal history of malignant neoplasm of other parts of uterus
Z85.43	Personal history of malignant neoplasm of ovary
Z85.44	Personal history of malignant neoplasm of other female genital organs
Z85.528	Personal history of other malignant neoplasm of kidney
Z85.53	Personal history of malignant neoplasm of renal pelvis
Z85.841	Personal history of malignant neoplasm of brain
Z85.848	Personal history of malignant neoplasm of other parts of nervous tissue

Reviews, Revisions, and Approvals	Date	P&T Approval Date
CP.PHAR.93.Avastin policy converted to new template; incorporates Avastin content from CP.PHAR.39 AMD Retinal Disorder Treatments. Added age and max dose; monotherapy defined as “other anti-VEGF drugs;” removed requests for documentation. References: removed 2008 Genentech letter regarding infections correlating with Avastin intravitreal use as it is no longer available.	03.16	09.16
Updated coding. Updated disclaimer language.	09.16	09.16
New FDA labeled indication added: Platinum-sensitive epithelial ovarian, fallopian tube, or primary peritoneal cancer. Doses removed. Under renal cell carcinoma, FDA approved use, added 2a/2b subtypes to interferon alpha. Safety criteria limited to black box warnings precluding initiation of therapy. Off-label ocular use is edited to follow supported uses in Micromedex and Clinical Pharmacology (i.e., AMD secondary to choroidal neovascularization, macular edema secondary to branch/central retinal vein occlusion or diabetes, choroidal retinal neovascularization secondary to pathologic myopia or angioid streaks, diabetic retinopathy, retinopathy of prematurity). Choroidal neovascularization associated with no known cause or with inflammation or ocular histoplasmosis syndrome is removed but may be requested under the Global Biopharm policy. Approval duration lengthened to 6 and 12 months. Added ICD-10 appropriate code ranges for eye conditions that now have a new 6 <sup>th</sup> or 7 <sup>th</sup> digit indicating the specific eye.	03.17	04.17

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
<p>1Q18 annual review: Policies combined from Medicaid and commercial New policy for HIM Specialist involvement in care added to all indications Added specific criteria for off-label uses for ophthalmic indications Added allowable off-label oncology indications as reflected in the NCCN compendium. Added 2018 codes H44.2A1-H44.2A3 References reviewed and updated</p>	11.20.17	02.18
<p>4Q 2018 annual review: added Mvasi to the policy; added NCCN Category 2A recommended off-label uses: AIDs-related Kaposi sarcoma, anaplastic gliomas, intracranial and spinal ependymoma, infiltrative supratentorial astrocytoma/oligodendroglioma, medulloblastoma; references reviewed and updated.</p>	07.31.18	11.18
<p>Added ICD-10 codes C21.8, C33, and C46.0-C46.9</p>	03.15.19	
<p>Added the following ICD-10 codes for diabetic retinopathy: E08.3521 – E08.3529, E08.3531- E08.3539, E08.3541 – E08.3549, E08.3551 – E08.3559, E08.3591- E08.3599, E09.3521 - E09.3529, E09.3531 – E09.3539, E09.3541 – E09.3549, E09.3551 – E09.3559, E09.3591 – E09.3599, E10.3521 – E10.3529, E10.3531 – E10.3539, E10.3541 – E10.3549, E10.3551 – E10.3559, E10.3591 – E10.3599, E11.3521 – E11.3529, E11.3531 – E11.3539, E11.3541 – E11.3549, E11.3551 – E11.3559, E11.3591 – E11.3599, E13.3521 – E13.3529, E13.3531 – E13.3539, E13.3541 – E13.3549, E13.3551 – E13.3559, E13.3591 – E13.3599</p>	06.06.19	
<p>RT4: Added biosimilar, Zirabev, to the policy; references reviewed and updated.</p>	07.08.19	
<p>4Q 2019 annual review: added NCCN category 2A recommended off-label uses: meningioma, small bowel adenocarcinoma; added additional ICD-10 codes for meningioma per NCCN (D32.0–D32.9, D42.0–D42.9, I67.89); updated glioblastoma, cervical cancer, and epithelial ovarian, fallopian tube, or primary peritoneal cancer FDA-approved indications in approval criteria; updated references reviewed and updated.</p>	08.09.19	11.19
<p>Added HIM-Medical Benefit line of business; added redirection to Mvasvi for Avastin.</p>	12.23.19	
<p>Revised Avastin redirection to Mvasi or Zirabev for non-ophthalmology uses per SDC and prior clinical guidance; added HIM line of business; removed HIM-Medical Benefit line of business and non-formulary references related to the HIM line of business.</p>	02.19.20	
<p>Added requirement for redirection to Mvasi or Zirabev to Section II for continued therapy requests for non-ophthalmology uses; allowed</p>	04.20.20	05.20

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Bevacizumab, Bevacizumab-awwb, Bevacizumab-bvzr



Reviews, Revisions, and Approvals	Date	P&T Approval Date
by-passing of redirection if state regulations do not allow step therapy in Stage IV or metastatic cancer settings.		

### **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. The Health Plan 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. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

## CLINICAL POLICY

Bevacizumab, Bevacizumab-awwb, Bevacizumab-bvzr



This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

### **Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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