Prior Authorization Review Panel

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CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 02/01/2020**
Policy Number: PA.CP.PHAR.93	**Effective Date: 01/01/2018** **Revision Date: 01/15/2020**
Policy Name: Bevacizumab (Avastin, Mvasi, Zirabev)	

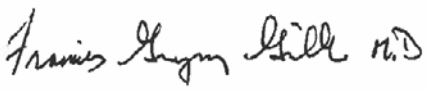
Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL** - *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

Added biosimilar, Zirabev, to the policy; 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; added redirection to Mvasvi for Avastin; references reviewed and updated.

Name of Authorized Individual (Please type or print): **Francis G. Grillo, MD**	**Signature of Authorized Individual:** 

Clinical Policy: Bevacizumab (Avastin, Mvasi, Zirabev)

Reference Number: PA.CP.PHAR.93
Effective Date: 01/18
Last Review Date: 01/2020

Coding Implications
Revision Log

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, with intravenous 5-fluorouracil (5-FU)-based chemotherapy for first- or second-line treatment
- Metastatic colorectal cancer, 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
It is the policy of Pennsylvania Health and Wellness that Avastin is **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. 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. 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 ≥ 18 years;
5. For Avastin requests, medical justification supports inability to use Mvasi (e.g., contraindications to the excipients);
   **Prior authorization may be required for Mvasi*
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: 6 months

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

1. Diagnosis of one of the following conditions:
   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 (e.g., contraindications to the excipients);
   **Prior authorization may be required for Mvasi*
1. 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: 6 months

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

1. Diagnosis of one of the following conditions:
   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. For Avastin requests, medical justification supports inability to use Mvasi (e.g., contraindications to the excipients);
   **Prior authorization may be required for Mvasi*
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: 6 months

D. Other Non-FDA Approved Indications (off-label) – Refer to the off-label use policy: PA.CP.PMN.53

II. Continued Approval

A. All Indications (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
1. Member is responding positively to therapy;
2. 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: 12 months

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PMN.53

III. 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
Metastatic carcinoma of the colon or rectum		
FOLFOX4 = Infusional 5-FU/leucovorin/ oxaliplatin	Oxaliplatin 85 mg/m^2 IV over 2 hours day 1; leucovorin 200 mg/m^2 IV over 2 hours days 1 & 2, followed by 5-FU 400 mg/m^2 IV bolus over 2-4 minutes, followed by 600 mg/m^2 IV 5-FU continuous infusion over 22 hours on days 1 & 2. Repeat cycle every 14 days.	Varies
FOLFIRI = Infusional 5-FU/ leucovorin/Camptosar® (irinotecan)	Camptosar 180 mg/m^2 IV over 90 minutes day 1; Leucovorin 400 mg/m^2 IV over 2 hours day 1 followed by 5-FU 400 mg/m^2 IV bolus over 2-4 minutes, followed by 2.4 gm/m^2 IV 5-	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	FU continuous infusion over 46 hours. Repeat cycle every 14 days.	
capecitabine (Xeloda®)	2500 mg/m^2 PO BID for 2 weeks; repeat cycles of 2 weeks on and 1 week off. For patients who cannot tolerate intensive therapy.	Varies
NSCLC		
cisplatin carboplatin paclitaxel docetaxel vinorelbine gemcitabine etoposide irinotecan vinblastine mitomycin ifosfamide pemetrexed disodium (Alimta®) (2nd line)	Various doses	Varies
Ovarian Cancer		
carboplatin and paclitaxel	Carboplatin dosed at an area under the curve (AUC) of 5-7.5 and paclitaxel 175 mg/m^2 IV over 3 hours given every 3 weeks for 6 courses.	Varies
docetaxel taxotere and carboplatin	Docetaxel, 60-75 mg/m^2 IV over 1 hour plus carboplatin dosed at AUC of 5 to 6 every 3 weeks.	Varies
Glioblastoma Multiforme		
temozolomide (Temodar®)	Maintenance phase cycles: 150 mg-200 mg/m² PO days 1-5. Repeat every 28 days.	Varies
Cervical Cancer		
cisplatin/paclitaxel	Paclitaxel: 135 mg/m^2 IV as a continuous infusion over 24 hours day 1 Cisplatin: 50 mg/m^2 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^2/day IV on days 1, 2, and 3	Varies

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

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.

IV. 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

Indication	Dosing Regimen	Maximum Dose
Non-squamous, non-small cell lung cancer	15 mg/kg IV infusion every 3 weeks with carboplatin/paclitaxel	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks
Ovarian cancer	15 mg/kg IV infusion every 3 weeks	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks
Platinum resistant ovarian cancer	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 IV every 2 weeks

V. Product Availability

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

VI. References

1. Avastin Prescribing Information. South San Francisco, CA: Genentech, Inc. June 2019. Available at: 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. Accessed September 30, 2019.
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; January 2015. Available at: www.aao.org/ppp. Accessed August 9, 2019.
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. 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. Accessed August 9, 2019.

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
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
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 – E093519	Drug or chemical induced diabetes mellitus with diabetic retinopathy with macular edema
E10.311, E10.3211 – E10.3219, E10.3311 – E10.3319,	Type 1 diabetes mellitus with diabetic retinopathy with macular edema

ICD-10-CM Code	Description
E10.3411 – E10.3419, E10.3511 – E10.3519	
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
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

ICD-10-CM Code	Description
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	Approval Date
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. Approval duration lengthened to 6 and 12 months. References reviewed and updated		
3Q 2019 annual review: No changes per Statewide PDL implementation 01/01/2020	07/17/19	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/30/19	
Added biosimilar, Zirabev, to the policy; 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; added redirection to Mvasvi for Avastin; references reviewed and updated.	01/2020	