Clinical Policy: Bevacizumab (Avastin)

Reference Number: PA.CP.PHAR.93
Effective Date: 01/18
Last Review Date: 07/18

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness ® clinical policy for bevacizumab (Avastin®).

FDA Approved Indication(s)
Avastin is indicated:

- For the treatment of metastatic colorectal cancer, with intravenous 5-fluorouracil (5-FU)-based chemotherapy for first- or second-line treatment
- For the treatment of metastatic colorectal cancer, with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line Avastin containing regimen
- For the treatment of non-squamous non-small cell lung cancer, with carboplatin and paclitaxel for first line treatment of unresectable, locally advanced, recurrent, or metastatic disease
- For the treatment of glioblastoma, as a single agent for adult patients with progressive disease following prior therapy
  - Effectiveness is based on improvement in objective response rate. There are no data available demonstrating improvement in disease-related symptoms or survival with Avastin.
- For the treatment of metastatic renal cell carcinoma in combination with interferon alfa
- For the treatment of cervical cancer, in combination with paclitaxel and cisplatin or paclitaxel and topotecan in persistent, recurrent, or metastatic disease.
- For the treatment of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer that is
  - Platinum-resistant in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan,
  - Platinum-sensitive in combination with carboplatin and paclitaxel or in combination with carboplatin and gemcitabine, followed by Avastin as a single agent

Limitation(s) of use: Avastin is 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 progressive 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;
   f. For epithelial ovarian, fallopian tube, or primary peritoneal cancer, disease is persistent, recurrent, or metastatic;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. 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*).

Approval duration: 6 months

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

1. Diagnosis of one of the following conditions:
   a. Breast cancer;
   b. Endometrial carcinoma;
   c. Malignant pleural mesothelioma;
   d. Primary central nervous system cancers;
   e. Soft tissue sarcoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

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. Request meets one of the following (a or b):
   a. Dose does not exceed 2.5 mg/dose;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval Duration: 6 months

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*).

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

Background

Description/Mechanism of Action:

Bevacizumab binds vascular endothelial growth factor (VEGF) and prevents the interaction of VEGF to its receptors (Flt-1 and KDR) on the surface of endothelial cells. The interaction of VEGF with its receptors leads to endothelial cell proliferation and new blood vessel formation in *in vitro* models of angiogenesis. Administration of bevacizumab to xenotransplant models of colon cancer in nude (athymic) mice caused reduction of microvascular growth and inhibition of metastatic disease progression.

Formulations:

Avastin: Intravenous solution: 100 mg/4 mL (4 mL); 400 mg/16 mL (16 mL)

Appendices

Appendix A: Abbreviation Key

5-FU/LV: fluorouracil, leucovorin
5-FU: fluorouracil
CapeOX: capecitabine, oxaliplatin
FOLFIRI: fluorouracil, leucovorin, irinotecan
FOLFOX: fluorouracil, leucovorin, oxaliplatin
FOLFOXIRI: fluorouracil, leucovorin, oxaliplatin, irinotecan
VEGF: vascular endothelial growth factor

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

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
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
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

ICD-10-CM Code	Description
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
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, 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

ICD-10-CM Code	Description
H40.50X0-H40.53X4	Glaucoma secondary to other eye disorders [associated with vascular disorders of eye]
H44.20-H44.23	Degenerative myopia
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	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		

References

1. Avastin. Prescribing Information. South San Francisco, CA: Genentech, Inc. December 2016. Available at: www.avastin.com. Accessed November 20, 2017.
2. Bevacizumab. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed November 20, 2017.
3. Bevacizumab. In: Micromedex. Ann Arbor, MI: Truven Health Analytics; 2013. Available from: www.micromedexsolutions.com. Accessed November 20, 2017.
4. Bevacizumab. In: Clinical Pharmacology. Tampa, FL: Gold Standard; 2008. Available at www.clinicalpharmacology.com. Accessed November 20, 2017.
5. Bevacizumab. In: Lexicomp. Hudson, OH: Wolters Kluwer; 2016. Available at www.online.lexi.com. Accessed November 20, 2017.
6. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; 2015. Available at www.aao.org/ppp. Accessed November 20, 2017.

7. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Diabetic Retinopathy. San Francisco, CA: American Academy of Ophthalmology; 2016. Available at www.aao.org/ppp. Accessed November 20, 2017.
8. 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 November 20, 2017.