Clinical Policy: Bevacizumab (Avastin)

Reference Number: PA.CP.PHAR.93
Effective Date: 01/18
Last Review Date: 04/17

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®).

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. Colorectal Cancer (must meet all):

1. Age ≥ 18 years;
2. Meets a or b:
   a. FDA approved use:
      i. Colorectal cancer (a or b):
         a) Primary or subsequent therapy for metastatic disease:
            1) In combination with 5-FU-based therapy*;
         b) Subsequent therapy for metastatic disease:
            1) In combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based therapy* after disease progression on a first-line Avastin-containing regimen;
   b. Off-label NCCN approved use:
      i. Colorectal cancer (a or b):
         a) Primary or subsequent therapy for unresectable, metastatic or medically inoperable disease (1, 2 or 3):
            1) In combination with capecitabine, FOLFOX, FOLFIRI, CapeOX, FOLFOXIRI, or 5-FU/LV*;
            2) In combination with irinotecan;
            3) In combination with irinotecan and oxaliplatin;
         b) Adjuvant therapy for resectable metastases:
            1) In combination with capecitabine, FOLFOX, FOLFIRI, CapeOX, FOLFOXIRI, or 5-FU/LV*;
      ii. Rectal cancer:
         a) Primary therapy for resectable disease classified as either (T3/N0/M0 [stage IIA]) or (anyT/N1-2/M0 [stage III)**:
            1) In combination with capecitabine, FOLFOX, FOLFIRI, FOLFOXIRI, CapeOX, or 5-FU/LV*;
3. Member's history is negative for the following:
   a. Serious hemorrhage or recent hemoptysis;
   b. Surgery within the last 28 days and unhealed surgical wounds.

**Examples of fluoropyrimidines: Capecitabine, floxuridine, fluorouracil (5-FU); examples of fluoropyrimidine-based regimens: 5-FU/LV (fluorouracil, leucovorin); FOLFOX (5-FU, leucovorin,*

oxaliplatin); FOLFIRI (5-FU, leucovorin, irinotecan); FOLFOXIRI (5-FU, leucovorin, oxaliplatin, irinotecan); CapeOX (capecitabine, oxaliplatin).
***American Joint Committee on Cancer (TNM staging classification (7th ed., 2010) as reported in NCCN Colon and Rectal Cancer: T (primary tumor characteristics), N (regional lymph node status), M (metastasis status).*

Approval duration: 6 months

B. Non-Squamous Non-Small Cell Lung Cancer (must meet all):
1. Age ≥ 18 years;
2. Non-squamous non-small cell lung cancer;
3. Meets a or b:
   a. FDA approved use:
      i. Primary therapy for unresectable, locally advanced, recurrent or metastatic disease:
         a) In combination with carboplatin and paclitaxel;
   b. Off-label NCCN recommended use (i or ii):
      i. Primary or subsequent therapy for unresectable, locally advanced, recurrent or metastatic disease (a, b, c or d):
         a) In combination with carboplatin and paclitaxel;
         b) In combination with carboplatin and pemetrexed;
         c) In combination with pemetrexed;
         d) In combination with cisplatin and pemetrexed;
      ii. Continuation maintenance therapy (if prior Avastin use associated with achievement of tumor response or stable disease) (a or b):
         a) As single agent;
         b) In combination with pemetrexed;
4. Member's history is negative for the following:
   a. Serious hemorrhage or recent hemoptysis;
   b. Surgery within the last 28 days and unhealed surgical wounds.

Approval duration: 6 months

C. Glioblastoma (must meet all):
1. Age ≥ 18 years;
2. Glioblastoma;
3. Meets a or b:
   a. FDA approved use:
      i. Subsequent therapy for recurrent or progressive disease;
         a) As single agent;
   b. Off-label NCCN recommended use:
      i. Subsequent therapy for recurrent or progressive disease:
         a) In combination with irinotecan, carmustine, lomustine, temozolomide, or carboplatin;
4. Member's history is negative for the following:
   a. Serious hemorrhage or recent hemoptysis;

b. Surgery within the last 28 days and unhealed surgical wounds.

Approval duration: 6 months

D. Renal Cell Carcinoma (must meet all):
1. Age ≥ 18 years;
2. Renal cell carcinoma;
3. Meets a or b:
   a. FDA approved use:
      i. Metastatic disease:
         a) In combination with interferon alfa-2a/2b;
   b. Off-label NCCN recommended use:
      i. Relapsed or stage IV (advanced or metastatic) disease (a, b or c):
         a) Clear cell histology - primary therapy:
            1) In combination with interferon alfa-2b;
         b) Clear cell histology - subsequent therapy:
            1) As single agent;
         c) Non-clear cell histology:
            1) As single agent;
4. Member's history is negative for the following:
   a. Serious hemorrhage or recent hemoptysis;
   b. Surgery within the last 28 days and unhealed surgical wounds.

Approval duration: 6 months

E. Carcinoma of the Cervix (must meet all):
1. Age ≥ 18 years;
2. Cervical carcinoma;
3. Meets a or b:
   a. FDA approved use:
      i. Persistent, recurrent or metastatic disease (a or b):
         a) In combination with paclitaxel and cisplatin;
         b) In combination with paclitaxel and topotecan;
   b. Off-label NCCN recommended use:
      i. Persistent, recurrent or metastatic disease (a or b):
         a) Primary therapy (1 or 2):
            1) In combination with carboplatin;
            2) In combination with topotecan;
         b) Subsequent therapy:
            1) As single agent;
4. Member's history is negative for the following:
   a. Serious hemorrhage or recent hemoptysis;
   b. Surgery within the last 28 days and unhealed surgical wounds.

Approval duration: 6 months

F. Epithelial Ovarian/Fallopian Tube/Primary Peritoneal Cancer (must meet all):
1. Age ≥ 18 years;
2. Meets a or b:
   a. FDA approved use (a or b):
      i. Epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer:
         a) Persistent/recurrent platinum-resistant disease:
            1) In combination with paclitaxel;
            2) In combination with pegylated liposomal doxorubicin;
            3) In combination with topotecan;
         b) Persistent/recurrent platinum-sensitive disease:
            1) In combination with carboplatin and paclitaxel;
            2) In combination with carboplatin and gemcitabine;
            3) As single agent;
   b. Off-label NCCN recommended use (i, ii, iii, iv):
      i. Epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer:
         a) Persistent/recurrent disease:
            1) As single-agent;
         b) Unresectable disease – primary therapy:
            1) In combination with carboplatin and paclitaxel;
         c) Stage II-IV disease post completion surgery* - adjuvant therapy:
            1) In combination with carboplatin and paclitaxel;
      ii. Granulosa cell tumor** (relapsed stage II-IV disease) – subsequent therapy:
         a) As single-agent;
      iii. Serous/endometrioid epithelial carcinoma (stage II-IV low-grade [grade 1]) - adjuvant therapy:
         a) In combination with carboplatin and paclitaxel;
      iv. Mucinous carcinoma of the ovary (stage II-IV) - adjuvant therapy:
         a) In combination with carboplatin and paclitaxel;
3. Member's history is negative for the following:
   a. Serious hemorrhage or recent hemoptysis;
   b. Surgery within the last 28 days and unhealed surgical wounds.

**Follow-up surgery performed if fertility-conserving strategies are no longer desired.*
***A type of malignant sex cord-stromal tumor.*

Approval duration: 6 months

G. Other diagnoses/indications: Refer to PA.CP.PHAR.57 - Global Biopharm Policy.
1. Oncology: The following NCCN recommended uses meeting NCCN categories 1, 2a or 2b are approved per the PA.CP.PHAR.57 Global Biopharm Policy:
   a. Age ≥ 18 years;
      i. Breast cancer;
      ii. Endometrial carcinoma;
      iii. Malignant pleural mesothelioma;
      iv. Primary central nervous system cancers (a or b):
         a) Adult intracranial and spinal ependymoma (excluding subependymoma);

b) Anaplastic glioma;
v. Soft tissue sarcoma (a or b):
a) Angiosarcoma;
b) Solitary fibrous tumor/hemangiopericytoma;

2. Ophthalmology (intravitreal administration):
   a. Retinopathy of prematurity;
   b. Age ≥ 18 years:
      i. Neovascular glaucoma;
      ii. Neovascular (wet) age-related macular degeneration;
      iii. Diabetic retinopathy;
      iv. Macular edema secondary to (a or b):
         a) Branch or central retinal vein occlusion;
         b) Diabetes;
      v. Choroidal/retinal neovascularization secondary to (a or b):
         a) Pathologic myopia;
         b) Angioid streaks;
3. Member's current history is negative for the following:
   a. Serious hemorrhage or recent hemoptysis;
   b. Surgery within the last 28 days and unhealed surgical wounds.

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;
2. Documentation of positive response to therapy (e.g.: no disease progression, not experiencing unacceptable toxicity);
3. If use is ophthalmic, evidence of detained neovascularization or improvement in visual acuity.

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.PHAR.57 – Global Biopharm Policy.

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)

FDA Approved Indications:
Avastin is a VEGF-specific angiogenesis inhibitor/solution for intravenous infusion indicated for the treatment of:

- Metastatic colorectal cancer, with intravenous 5-fluorouracil–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 Avastin containing regimen.
- Non-squamous non-small cell lung cancer, with carboplatin and paclitaxel for first line treatment of unresectable, locally advanced, recurrent or metastatic disease.
- Glioblastoma, as a single agent for adult patients with progressive disease following prior therapy. Effectiveness based on improvement in objective response rate. No data available demonstrating improvement in disease-related symptoms or survival with Avastin.
- Metastatic renal cell carcinoma with interferon alfa.
- Cervical cancer, in combination with paclitaxel and cisplatin or paclitaxel and topotecan in persistent, recurrent, or metastatic disease.
- Platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, in combination with paclitaxel, pegylated liposomal doxorubicin or topotecan.
- Platinum-sensitive recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, in combination with carboplatin and paclitaxel or in combination with carboplatin and gemcitabine, followed by Avastin as a single agent.

*Limitation of use: Avastin is not indicated for adjuvant treatment of colon cancer.

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
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

ICD-10-CM Code	Description
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
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

ICD-10-CM Code	Description
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

References

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