CLINICAL MEDICAL POLICY	
Policy Name:	Avastin® (bevacizumab)
Policy Number:	MP-030-MD-PA
Approved By:	Medical Management
Provider Notice Date:	07/01/2017
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Products:	Pennsylvania Medicaid
Application:	All participating hospitals and providers
Page Number(s):	1 of 8

DISCLAIMER

Gateway Health℠ (Gateway) medical policy is intended to serve only as a general reference resource regarding payment and coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT

Gateway Health℠ provides coverage for Avastin® (bevacizumab) under the medical benefits of the Company's Medicaid products for cervical cancer, colorectal cancer, glioblastoma, non-squamous non-small cell lung cancer, ovarian cancer, and renal cancer when medically necessary.

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

(Current applicable Pennsylvania HealthChoices Agreement Section V. Program Requirements, B. Prior Authorization of Services, 1. General Prior Authorization Requirements.)

DEFINITIONS

Avastin – A recombinant human monoclonal antibody that binds to and inhibits the biologic activity of human vascular endothelial growth factor (VEGF) to thereby inhibit cell proliferation and new blood vessel formation.

PROCEDURES

1. Avastin is considered medically necessary as an intravenous injection when the patient meets the following criteria:
   A. Cervical Cancer
      1) The patient is aged 18 years or older; AND
      2) The prescribing physician must be a Hematologist or Oncologist; AND
      3) The disease is a persistent, recurrent, or metastatic disease that is not amenable to curative treatment with surgery or radiotherapy; AND
      4) The drug will be used in combination with paclitaxel and cisplatin or paclitaxel and topotecan for persistent, recurrent, or metastatic disease; AND
      5) The dose does not exceed 15 mg/kg IV every 3 weeks, with paclitaxel and cisplatin or paclitaxel and topotecan.

   B. Colorectal Cancer
      1) The patient is aged 18 years or older; AND
      2) The prescribing physician must be a Hematologist or Oncologist; AND
      3) The disease is metastatic; AND
      4) The drug will be used in combination with intravenous 5-fluorouracil (IFL) based chemotherapy for first- or second-line treatment; OR
      5) The drug will be used in combination with fluoropyrimidine-irinotecan or fluoropyrimidine-oxaliplatin based chemotherapy for second-line treatment in patients who have progressed on a first-line Avastin-containing regimen; AND
      6) The dose does not exceed
         a) 5 mg/kg IV every 2 weeks with bolus-IFL;
         b) 10 mg/kg IV every 2 weeks with FOLFOX4;
         c) 5 mg/kg IV every 2 weeks or 7.5 mg/kg IV every 3 weeks with fluoropyrimidine-irinotecan or fluoropyrimidine-oxaliplatin based chemotherapy after progression on a first-line Avastin-containing regimen

   C. Recurrent Glioblastoma
      1) The patient is aged 18 years or older; AND
      2) The prescribing physician must be a Hematologist or Oncologist; AND
      3) The drug will be used as a single agent for adult patients with progressive disease following prior therapy; AND
      4) The dose does not exceed 10 mg/kg IV every 2 weeks.

   D. Non-Squamous Non-Small Cell Lung Cancer
      1) The patient is aged 18 years or older; AND
      2) The prescribing physician must be a Hematologist or Oncologist; AND
      3) The drug will be used in combination with carboplatin and paclitaxel for first-line treatment of unresectable, locally advanced, recurrent, or metastatic disease; AND
      4) The dose does not exceed 15 mg/kg IV every 3 weeks with carboplatin/paclitaxel.

E. Ovarian Cancer
    1) The patient is aged 18 years or older; AND
    2) The prescribing physician must be a Hematologist or Oncologist; AND
    3) The diagnosis is recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer; AND
    4) The drug will be used for platinum-resistant cancer in combination with paclitaxel, pegylated liposomal doxorubicin or topotecan;
    OR
    5) The drug will be used for platinum-sensitive cancer in combination with carboplatin and paclitaxel or in combination with carboplatin and gemcitabine followed by Avastin as a single agent paclitaxel; AND
    6) The dosage does not exceed:
        d) Platinum-resistant:
            I. 10 mg/kg IV every 2 weeks with paclitaxel, pegylated liposomal doxorubicin or weekly topotecan
            II. 15 mg/kg every 3 weeks with topotecan
        e) Platinum-sensitive:
            I. 15 mg/kg every 3 weeks in combination with carboplatin/paclitaxel for 6 to 8 cycles, followed by 15 mg/kg every three weeks as a single agent; OR
            II. 15 mg/kg every three weeks in combination with carboplatin/gemcitabine for 6 to 10 cycles, followed by 15 mg/kg every three weeks as a single agent

F. Metastatic Renal Cell Carcinoma
    1) The patient is aged 18 years or older; AND
    2) The prescribing physician must be a Hematologist or Oncologist; AND
    3) The drug will be used in combination with interferon-alfa; AND
    4) The dose does not exceed 10 mg/kg IV every 2 weeks with interferon-alfa

2. Contraindications
   None

3. Precautions:
   Gastrointestinal Perforation: Occurs in up to 3.2% of Avastin-treated patients. Discontinue Avastin for gastrointestinal perforation.

   Surgery and Wound Healing Complications: Discontinue in patients with wound dehiscence. Discontinue at least 28 days prior to elective surgery. Do not initiate Avastin for at least 28 days after surgery and until the surgical wound is fully healed.

   Hemorrhage: Severe or fatal hemorrhage, hemoptysis, gastrointestinal bleeding, CNS hemorrhage, and vaginal bleeding are increased in Avastin-treated patients. Do not administer Avastin to patients with serious hemorrhage or recent hemoptysis.

4. When Avastin is not covered
   Avastin is not covered for conditions other than those listed above because the scientific evidence has not been established.

   Coverage may be provided for any non-FDA labeled indication if it is determined that the use is a medically accepted indication supported by nationally recognized pharmacy compendia or peer-reviewed medical literature for treatment of the diagnosis (es) for which it is prescribed. These requests will be reviewed on a case-by-case basis to determine medical necessity.

   When non-formulary criteria are not met, the request will be forwarded to a Medical Director for review. The physician reviewer must override criteria when, in their professional judgment, the requested medication is medically necessary.

5. Post-payment Audit Statement
   The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Gateway Health℠ at any time pursuant to the terms of your provider agreement.

6. Place of Service
   The place of service for the administration of Avastin is outpatient.

GOVERNING BODIES APPROVAL

In October 2006, the FDA approved Avastin for first-line treatment of patients with unresectable, locally advanced, recurrent, or metastatic non-squamous non-small cell lung cancer in combination with carboplatin and paclitaxel.

In February 2008, the FDA granted accelerated approval for Avastin in combination with paclitaxel chemotherapy for the treatment of chemo-naive patients with metastatic human epidermal growth factor receptor 2 (HER2)-negative breast cancer. In December 2010, the FDA proposed withdrawing the Avastin indication to treat women with metastatic breast cancer following an expert-panel review of clinical data supporting this indication. The panel concluded that there is not enough evidence that the drug is safe and effective for this indication. The announcement stated that the panel decision would not have any immediate effect on the approval of Avastin to treat metastatic breast cancer and there would be no change to product labeling. Since the marketing approval remains in effect, patients with breast cancer would still have access to the drug until a final decision has been made. As of January 2011, Genentech has notified the FDA of its request for a Notice of Opportunity for a Hearing regarding the proposed indication removal. On November 18, 2011, the FDA officially removed the Avastin indication for metastatic breast cancer because the drug has not proven to be safe and effective for that indication.

In May 2009, the FDA granted approval of Avastin for use in glioblastoma, as a single agent, for patients with progressive disease following prior therapy.

In July 2009, the FDA granted approval of Avastin for use in combination with interferon-alfa for the treatment of renal cell carcinoma.

In August 2014, Genentech received FDA approval for persistent, recurrent, or metastatic cervical cancer in combination with paclitaxel and cisplatin OR paclitaxel and topotecan.

In November 2014, Avastin was FDA approved for treatment in patients with platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan.

The safety, effectiveness, and pharmacokinetic profile of Avastin in pediatric patients have not been established. In published literature reports, cases of non-mandibular osteonecrosis have been observed in patients under the age of 18 years who have received Avastin. Avastin is not approved for use in patients under the age of 18 years.

CODING REQUIREMENTS

Procedure Codes

HCPCS Codes	Description
C9357	Injection, bevacizumab, 0.25 mg
J9035	Injection, bevacizumab, 10 mg

Diagnosis Codes

ICD 10 Codes	Description
C17.0	Malignant neoplasm of duodenum
C17.1	Malignant neoplasm of jejunum
C17.2	Malignant neoplasm of ileum
C17.3	Meckel's diverticulum, malignant
C17.8	Malignant neoplasm of overlapping sites of small intestine
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.0	Malignant neoplasm of anus, unspecified
C21.1	Malignant neoplasm of anal canal
C21.2	Malignant neoplasm of cloacogenic zone
C21.8	Malignant neoplasm of overlapping sites of rectum, anus, and anal canal
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung

C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C38.4	Malignant neoplasm of pleura
C45.0	Mesothelioma of pleura
C48.0	Malignant neoplasm of retroperitoneum
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C53.0	Malignant neoplasm of endocervix
C53.1	Malignant neoplasm of exocervix
C53.8	Malignant neoplasm of overlapping sites of cervix uteri
C53.9	Malignant neoplasm of cervix uteri, unspecified
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.9	Malignant neoplasm of unspecified ovary
C57.00	Malignant neoplasm of unspecified fallopian tube
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
C71.0	Malignant neoplasm of cerebrum, except lobes and ventricles
C71.1	Malignant neoplasm of frontal lobe
C71.2	Malignant neoplasm of temporal lobe
C71.3	Malignant neoplasm of parietal lobe
C71.4	Malignant neoplasm of occipital lobe
C71.5	Malignant neoplasm of cerebral ventricle
C71.6	Malignant neoplasm of cerebellum
C71.7	Malignant neoplasm of brain stem
C71.8	Malignant neoplasm of overlapping sites of brain
C71.9	Malignant neoplasm of brain, unspecified
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung

C78.02	Secondary malignant neoplasm of left lung
C78.30	Secondary malignant neoplasm of unspecified respiratory organ
C78.39	Secondary malignant neoplasm of other respiratory organs
C78.4	Secondary malignant neoplasm of small intestine
C78.5	Secondary malignant neoplasm of large intestine and rectum
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C79.00	Secondary neoplasm of unspecified kidney and renal pelvis
C79.01	Secondary neoplasm of right kidney and renal pelvis
C79.02	Secondary neoplasm of left kidney and renal pelvis
C79.60	Secondary neoplasm of unspecified ovary
C79.61	Secondary neoplasm of right ovary
C79.62	Secondary neoplasm of left ovary
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
Z85.43	Personal history of malignant neoplasm of ovary
Z85.528	Personal history of malignant neoplasm of kidney
Z85.841	Personal history of malignant neoplasm of brain

REIMBURSEMENT

Participating facilities will be reimbursed per their Gateway Health℠ contract.

POLICY SOURCE(S)

Avastin® (bevacizumab) [package insert]. Genetech, Inc., 2016. Accessed on January 12, 2017 and available at: https://www.gene.com/download/pdf/avastin_prescribing.pdf.

Bevacizumab. In: Micromedex 2.0 online. Ann Arbor (MI): Truven Health Analytics.

National Comprehensive Cancer Network® NCCN Clinical Practice Guidelines in Oncology™. Accessed on 12/28/2016 and available at: http://www.nccn.org/index.asp.

- NCCN Guidelines Version 1.2016: Cervical Cancer
- NCCN Guidelines Version 1.2017: Cervical Cancer
- NCCN Guidelines Version 2.2016: Colon Cancer
- NCCN Guidelines Version 1.2017: Colon Cancer
- NCCN Guidelines Version 2.2016: Uterine Neoplasms
- NCCN Guidelines Version 1.2016: Ovarian Cancer
- NCCN Guidelines Version 2.2017: Kidney Cancer
- NCCN Guidelines Version 4.2016: Non-Small Cell Lung Cancer

Aghajanian C, Sill MW, Darcy KM, et al. Phase II trial of bevacizumab in recurrent or persistent endometrial cancer: A Gynecologic Oncology Group Study. *J Clin Oncol* 2011; 29:2259-2265. Accessed on January 12, 2017 and available at: http://ascopubs.org/doi/pdf/10.1200/JCO.2010.32.6397.

Policy History

Date	
03/16/2017	Initial policy developed
06/21/2017	QI/UM Committee approval
08/01/2017	Provider effective date