Policy Title:	Avastin (bevacizumab) **ONCOLOGY ONLY** (Intravenous)		
		Department:	PHA
Effective Date:	01/01/2020		
Review Date:	9/18/2019, 1/29/20		
Revision Date:	9/18/2019, 1/29/20		

Purpose: To support safe, effective and appropriate use of Avastin (bevacizumab).

Scope: Medicaid, Exchange, Medicare-Medicaid Plan (MMP)

Policy Statement:

Avastin (bevacizumab) is covered under the Medical Benefit when used within the following guidelines for oncology indications. All retinal indications are covered without an authorization. Use outside of these guidelines may result in non-payment unless approved under an exception process.

Procedure:

Coverage of Avastin (bevacizumab) will be reviewed prospectively via the prior authorization process based on criteria below.

Initial Criteria :

- Patient must have no recent history of hemorrhage or hemoptysis (the presence of blood in sputum); AND
- Patient must not have had a surgical procedure within the preceding 28 days or have a surgical wound that has not fully healed; AND
- For new start to therapy, patient must have failure or intolerable side effects to a bevacizumab biosimilar product. Patients that are currently on treatment with Avastin (bevacizumab) can remain on treatment OR for MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

Colorectal Cancer (CRC)

- Not used as part of adjuvant treatment; AND
- Patient's disease is metastatic, unresectable, or advanced; AND
    - Used as first-line therapy; AND
        - In combination with a fluoropyrimidine-based regimen (e.g., 5-fluorouracil/5-FU or capecitabine); OR
        - In combination with irinotecan or irinotecan-based regimen after previous adjuvant FOLFOX or CapeOX within the past 12 months; OR

- Used as subsequent therapy; AND
  - In combination with a fluoropyrimidine-based regimen (e.g., 5-fluorouracil/5-FU or capecitabine); OR
  - In combination with irinotecan (if irinotecan was not previously used); OR
- Used for metastatic disease that has progressed on first-line bevacizumab containing regimen in combination with an irinotecan and/or oxaliplatin-based regimen (if not used first-line).

Non-Squamous Non-Small Cell Lung Cancer (NSCLC)

- Used as first-line therapy for:
  - Recurrent, locally advanced, unresectable, or metastatic disease in combination with carboplatin and paclitaxel; OR
  - Recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease) with EGFR, ALK negative or unknown, PD-L1 expression ≥ 50% and performance status (PS) ≤ 2 in combination with atezolizumab, carboplatin, and paclitaxel; OR
- Used for recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease) with PS ≤ 1 in combination with:
  - Carboplatin AND either paclitaxel or pemetrexed; OR
  - Cisplatin and pemetrexed; OR
  - Atezolizumab, carboplatin and paclitaxel; AND
    - Used as first-line therapy for genomic tumor aberration** (e.g., EGFR, ALK, ROS1, BRAF) negative or unknown and PD-L1<50% or unknown OR BRAF V600E-mutation positive; OR
    - Used as subsequent therapy for genomic tumor aberration** (e.g., EGFR, ALK, ROS1) positive and prior targeted therapy OR BRAF V600E-mutation positive OR PD-L≥ 50% and EGFR, ALK negative or unknown with no prior platinum-doublet chemotherapy; OR
- Used as continuation maintenance therapy with PS ≤ 2 AND
  - Bevacizumab must have been included in patient's first-line chemotherapy regimen for recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease); AND
  - Patient's disease has not progressed (achieved tumor response or stable disease) after first-line chemotherapy; AND
    - Used as a single agent; OR
    - Used in combination with pemetrexed if bevacizumab was previously used with a first-line pemetrexed/platinum chemotherapy regimen; OR
    - Used in combination with atezolizumab if bevacizumab was previously used first-line as part of atezolizumab/carboplatin/paclitaxel/bevacizumab regimen.

Cervical Cancer

- Patient's disease must be persistent, recurrent, or metastatic; AND
- Used in combination with paclitaxel AND either cisplatin, carboplatin, or topotecan.

Renal Cell Carcinoma (RCC)

- Patient must have metastatic or relapsed disease; AND
  - Must be used in combination with interferon alfa; OR
  - Must be used as a single agent in patients with non-clear cell histology; OR

- Used in combination with everolimus in patients with non-clear cell histology; OR
- Used in combination with erlotinib in patients with non-clear cell histology papillary disease including hereditary leiomyomatosis and renal cell cancer (HLRCC).

Central Nervous System (CNS) Cancer

- Used as a single agent OR in combination with one of the following: irinotecan, carmustine, lomustine, or temozolomide in patients with recurrent Glioblastomas

Ovarian Cancer

- Patient has malignant stage II-IV sex cord-stromal tumors; AND
  - Used as single agent therapy for relapsed disease; OR
- Patient has Epithelial or Fallopian Tube or Primary Peritoneal Cancers; AND
  - Patient has persistent or recurrent disease; AND
    - Bevacizumab has not been used previously; AND
    - Patient is not experiencing an immediate biochemical relapse (i.e., rising CA-125 without radiographic evidence of disease); AND
      - Used as a single agent; OR
      - If platinum sensitive, used in combination with carboplatin AND either gemcitabine or paclitaxel; OR
      - If platinum resistant, used in combination with one of the following: PEGylated liposomal doxorubicin, weekly paclitaxel, or topotecan; OR
  - Used as single agent maintenance therapy if used previously as part of combination therapy in patients with a partial or complete remission following primary therapy or following recurrence therapy for platinum-sensitive disease; OR
  - Used as neoadjuvant therapy for endometrioid or serous histology in combination with paclitaxel and carboplatin; AND
    - Patient has bulky stage III or IV disease or is a poor surgical candidate; OR
  - Used as primary therapy for endometrioid or serous histology in combination with paclitaxel and carboplatin; AND
    - Patient had an incomplete resection and/or has unresectable stage II-IV disease; OR
  - Used as adjuvant therapy in combination with paclitaxel and carboplatin; AND
    - Patient has stage II-IV disease of serous, endometrioid, mucinous carcinoma, or clear cell carcinoma histology; OR
    - Patient has borderline epithelial tumors with invasive implants; OR
- Used as adjuvant therapy in combination with carboplatin and paclitaxel in patients with stage I-IV carcinosarcoma (malignant mixed Müllerian tumors [MMMTs]).

Genomic Aberration Targeted Therapies (not all inclusive) **
Sensitizing EGFR mutation-positive tumors: • Erlotinib • Afatinib • Gefitinib • Osimertinib • Dacomitinib
ALK rearrangement-positive tumors: • Crizotinib • Ceritinib • Brigatinib • Alectinib • Lorlatinib
ROS1 rearrangement-positive tumors: • Crizotinib • Ceritinib
BRAF V600E-mutation positive tumors: • Dabrafenib/Trametinib
PD-L1 expression-positive tumors (>50%): • Pembrolizumab • Atezolizumab

Continuation of Therapy coverage:

- Patient continues to meet initial criteria; AND
- Tumor response with stabilization of disease or decrease in size of tumor or tumor spread; AND
- Patient is tolerating treatment with absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: gastrointestinal perforation, surgical/wound healing complications, hemorrhage, arterial and venous thromboembolic events (ATE & VTE), uncontrolled hypertension, posterior reversible encephalopathy syndrome (PRES), nephrotic syndrome, severe infusion reactions, ovarian failure, congestive heart failure (CHF), etc.; AND

Colorectal Cancer (additional renewal opportunity):

- Patient's disease has progressed on a first-line bevacizumab-containing regimen; AND
    - Used in combination with an irinotecan and/or oxaliplatin-based regimen (if not used first line)

CNS Cancers- symptom management (short-course therapy):

- May NOT be renewed

Ovarian cancer - Platinum sensitive disease or recurrence:

- Must be used as a single agent for maintenance therapy; OR

- Used in combination with chemotherapy, for completion of initial therapy, up to 10 cycles total

Non-squamous non-small cell lung cancer – continuation maintenance therapy:

- Bevacizumab must have been included in patient's 1st line chemotherapy; AND
- Patient must have an ECOG performance status ≤ 2; AND
    - Used as a single agent; OR
    - Used in combination with pemetrexed if bevacizumab was previously used with a first-line pemetrexed/platinum chemotherapy regimen; OR
    - Used in combination with atezolizumab if bevacizumab was previously used first-line as part of atezolizumab/carboplatin/paclitaxel/bevacizumab regimen

Dosage/Administration:

Indication	Dose (1 billable unit = 10 mg)	Maximum units
CRC	5 to 10 mg/kg every 2 weeks or 7.5 mg/kg every 3 weeks	170 billable units per 21 days 120 billable units per 14 days
NSCLC & Cervical Cancer	15 mg/kg every 3 weeks until disease progression or unacceptable toxicity	170 billable units per 21 days 120 billable units per 14 days
CNS Cancers	For disease treatment: 10 mg/kg every 2 weeks until disease progression or unacceptable toxicity For symptom management: 5-10 mg/kg every 2 weeks up to 12 weeks duration	170 billable units per 21 days 120 billable units per 14 days
RCC	10 mg/kg every 2 weeks until disease progression or unacceptable toxicity	170 billable units per 21 days 120 billable units per 14 days
Ovarian Cancer	Platinum-sensitive: 15 mg/kg every 3 weeks for up to 8 cycles when used with paclitaxel or up to 10 cycles when used with gemcitabine; followed by single-agent bevacizumab 15 mg/kg IV every 3 weeks until disease progression or unacceptable toxicity Platinum-resistant: 10 mg/kg every 2 weeks or 15 mg/kg every 3 weeks until disease progression or unacceptable toxicity	170 billable units per 21 days 120 billable units per 14 days
All Other Oncology Indications	5-10 mg/kg every 2 weeks OR 7.5-15 mg/kg every 3 weeks	170 billable units per 21 days 120 billable units per 14 days

Coverage durations:

- Initial coverage: 6 months
- Continuation of therapy coverage: 6 months

*** Requests will also be reviewed to National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) if applicable. ***

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of the billing code applicable for covered treatment options. The below table is provided for reference purposes and may not be all inclusive. Requests received with codes from the table below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT code is:

HCPCS/CPT Code	Description
J9035	Injection, bevacizumab, 10 mg

References:

1. Avastin [package insert]. South San Francisco, CA; Genentech; June 2019.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) bevacizumab. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2019.
3. Delishaj D, Ursino S, Pasqualetti F, et al. Bevacizumab for the Treatment of Radiation-Induced Cerebral Necrosis: A Systematic Review of the Literature. J Clin Med Res. 2017 Apr; 9(4): 273–280.
4. National Government Services, Inc. Local Coverage Article for BEVACIZUMAB (e.g., Avastin™) - Related to LCD L33394 (A52370). Centers for Medicare & Medicaid Services, Inc. Updated on 9/21/2018 with effective date 10/1/2018. Accessed January 2019.