AVASTIN (bevacizumab)

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<td>Akamai Advantage</td>
<td>10/01/2015</td>
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**POLICY**

**A. INDICATIONS**

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

**FDA-Approved Indications**

- Platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, in combination with paclitaxel, pegylated liposomal doxorubicin or topotecan for patients who received no more than 2 prior chemotherapy regimens
- Cervical cancer, in combination with paclitaxel and cisplatin or paclitaxel and topotecan in persistent, recurrent, or metastatic disease
- Metastatic colorectal cancer:
  - In combination with intravenous 5-fluorouracil-based chemotherapy for first- or second-line treatment
  - 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
- Non-squamous non-small cell lung cancer (NSCLC), 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
- Metastatic renal cell carcinoma with interferon alfa

**Compendial Uses**

- Breast cancer
- Central nervous system (CNS) cancers
  - Adult intracranial and spinal ependymoma
  - Anaplastic gliomas
- **Cervical cancer**
- Colon/rectal cancer
- Endometrial cancer
- **Malignant pleural mesothelioma**
- Non-small cell lung cancer
- Ovarian cancer
• Malignant sex cord-stromal tumors
• Renal cell carcinoma
• Soft tissue sarcoma
• Malignant pleural mesothelioma
• Ophthalmic-related disorders
  o Choroidal neovascularization (CNV)
  o Wet age-related macular degeneration (AMD)
  o Macular edema due to retinal vein occlusion (RVO)
  o Diabetic macular edema
  o Ocular neovascularization (choroidal, retinal, iris) associated with proliferative diabetic retinopathy
  o Neovascular glaucoma
  o Retinopathy of prematurity

B. REQUIRED DOCUMENTATION
The following information may be necessary to initiate the prior authorization review:
• All approvable oncologic diagnoses
  o Current oncology notes, clinical notes (including previous treatment history), and any pertinent pathology reports and/or imaging studies
• All approvable oncologic diagnoses for continuation therapy
  o Documentation demonstrating lack of disease progression on therapy
• Breast cancer
  o Human epidermal growth factor receptor 2 (HER2) test result
  o Hormone receptor (HR) test result
• NSCLC
  o Documentation of previous treatment history where applicable
  o Epidermal growth factor receptor (EGFR) mutation test result
  o ALK rearrangement test result
  o Tumor histology
• Renal cell carcinoma
  o Tumor histology

C. PRESCRIBER RESTRICTION
• All approvable oncologic diagnoses
  o Avastin must be prescribed by an oncologist.

D. CRITERIA FOR APPROVAL
1. Breast cancer
   Authorization of 3 months may be granted to members who are prescribed Avastin in combination with paclitaxel for the treatment of HER2-negative recurrent or metastatic breast cancer when members have ANY of the following types of disease:
   a. Symptomatic visceral disease
   b. Disease with visceral crisis
   c. HR-negative disease
   d. HR-positive disease refractory to endocrine therapy

2. Cervical cancer
Authorization of 3 months may be granted for the treatment of persistent, recurrent, or metastatic cervical cancer when Avastin is prescribed in ONE of the following regimens:

- Avastin, cisplatin and paclitaxel
- Avastin, carboplatin and paclitaxel
- Avastin, topotecan and paclitaxel

3. CNS cancer

3.1. Glioblastoma and anaplastic glioma

Authorization of 3 months may be granted to members who are prescribed Avastin in combination with irinotecan, carmustine, lomustine, or temozolomide, or as a single agent for recurrent or progressive disease.

3.2. Adult intracranial and spinal ependymoma (excludes subependymoma)

Authorization of 3 months may be granted to members who are prescribed Avastin as a single agent for disease progression.

4. Colorectal cancer

- Authorization of 3 months may be granted to members who are prescribed Avastin as therapy for T4b colorectal cancer prior to colectomy or rectal cancer stage II or III (T3, N0, M0; any T, N1-2, M0; or T4) and/or locally unresectable or medically inoperable disease and Avastin will be used in combination with capecitabine, FOLFIRI, FOLFOX, CapeOX, FOLFOXIRI, or 5-FU with leucovorin.

- Authorization of 3 months may be granted to members who are prescribed Avastin as perioperative (neoadjuvant/adjuvant/postoperative) therapy for resectable synchronous liver and/or lung metastases and Avastin will be used in combination with FOLFIRI**, FOLFOX**, or CapeOX**.

** CapeOX = capecitabine and oxaliplatin; FOLFIRI = leucovorin, fluorouracil, and irinotecan; FOLFOX = leucovorin, fluorouracil, and oxaliplatin; FOLFOXIRI = leucovorin, fluorouracil, oxaliplatin, and irinotecan.

- Authorization of 3 months may be granted to members who are prescribed Avastin as perioperative (neoadjuvant/perioperative/adjuvant/postoperative) therapy for resectable metastases metachronous metastases and Avastin will be used in combination with capecitabine, FOLFIRI, FOLFOX, CapeOX, FOLFOXIRI***, or 5-FU with leucovorin for members who were previously treated with chemotherapy.

*** FOLFOXIRI = leucovorin, fluorouracil, oxaliplatin, and irinotecan.

- Authorization of 3 months may be granted to members who are prescribed Avastin in combination with irinotecan or FOLFIRI for unresectable metastases with previous adjuvant FOLFOX or CapeOX therapy within the past 12 months.

- Authorization of 3 months may be granted to members who are prescribed Avastin in combination with capecitabine, FOLFIRI, FOLFOX, CapeOX, FOLFOXIRI, or 5-FU with
leucovorin for unresectable advanced or metastatic disease as initial therapy who can tolerate intensive therapy.

**e.f. Authorization of 3 months may be granted to members who are prescribed Avastin in combination with infusional 5-FU with leucovorin, or capecitabine for unresectable advanced or metastatic disease as initial therapy who CANNOT tolerate intensive therapy.**

**f.g. Authorization of 3 months may be granted when Avastin is prescribed after first progression of unresectable advanced or metastatic disease as ONE of the following:**

i. In combination with FOLFIRI or irinotecan for members who were previously treated with an oxaliplatin-based regimen,

ii. In combination with FOLFOX or CapeOX for members who were previously treated with an irinotecan-based regimen, OR

iii. In combination with FOLFOX, CapeOX, irinotecan, irinotecan and oxaliplatin, or FOLFIRI for members who were treated with 5-FU with leucovorin or capecitabine regimen.

CapeOX = capecitabine and oxaliplatin; FOLFIRI = leucovorin, fluorouracil, and irinotecan; FOLFOX = leucovorin, fluorouracil, and oxaliplatin; FOLFOXIRI = leucovorin, fluorouracil, oxaliplatin, and irinotecan.

5. **Endometrial cancer**
Authorization of 3 months may be granted to members who are prescribed Avastin as a single agent and who have progressed on prior cytotoxic chemotherapy.

6. **Ovarian cancer**
   6.1 **Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer**
   Authorization of 3 months may be granted to members who meet ALL of the following criteria:
   a. Member has persistent or recurrent disease.
   b. Member has not previously received Avastin.
   c. Avastin will be used as ONE of the following:
      i. As a single agent for platinum-sensitive or -resistant disease
      ii. In combination with liposomal doxorubicin, paclitaxel, or topotecan for platinum-resistant disease

   6.2 **Malignant sex cord-stromal tumors**
   Authorization of 3 months may be granted to members in clinical relapse with stage II-IV granulosa cell tumors.

7. **NSCLC**
   a. The disease is unresectable, locally advanced, recurrent, or metastatic.
   b. Member has ECOG performance status (PS) 0-1 (first-line/subsequent therapy) or PS 0-2 (continuation maintenance), tumors of non-squamous cell histology, and no history of recent hemoptysis.
   c. Authorization of 3 months may be granted to members who are prescribed Avastin in combination with carboplatin and paclitaxel or pemetrexed or with cisplatin and pemetrexed or carboplatin-based regimens who meet one of the following:
i. For tumors with negative/unknown EGFR mutations and negative/unknown ALK gene rearrangements, ROS1 rearrangements or PD-L1 expression (≥50%) Avastin will be used as a first-line therapy (see section d. below for continuation maintenance).

ii. For tumors with sensitizing EGFR mutation-positive tumors:
   1) Avastin will be used as a subsequent therapy with or without erlotinib AND
   2) Member experienced disease progression on has received prior erlotinib (Tarceva), or afatinib (Gilotrif), gefitinib (Iressa) or osimertinib (Tagrisso) therapy.

iii. For ALK-positive tumors:
   1) Avastin will be used as a subsequent therapy AND
   2) Member experienced disease progression on has received prior crizotinib (Xalkori), ceritinib (Zykadia) or alectinib (Alecensa) therapy.

iv. For ROS1-positive tumors:
   1) Avastin will be used as a subsequent therapy AND
   2) Member experienced disease progression on prior crizotinib (Xalkori) therapy.

v. For PD-L1 expression-positive (≥50%) tumors:
   1) Avastin will be used as a subsequent therapy AND
   2) Member experienced disease progression on prior pembrolizumab (Keytruda) therapy.

iv. Authorization of 3 months may be granted to members who are prescribed Avastin as a continuation maintenance therapy when ALL of the following criteria are met:
   i. The tumor is negative or unknown for both EGFR mutations and ALK rearrangements
   ii. Members have achieved tumor response or stable disease following first-line chemotherapy.
   iii. Avastin will be used as a single agent or in combination with pemetrexed if previously used with a first-line pemetrexed/platinum chemotherapy regimen.

8. Renal cell carcinoma
   Authorization of 3 months may be granted for the treatment of relapsed, metastatic or surgically unresectable stage IV renal cell carcinoma when Avastin will be used as ONE of the following:
   a. As a first-line therapy
      i. Avastin monotherapy for disease with non-clear cell histology OR
   b. As a subsequent therapy
      Avastin monotherapy for disease with non-clear cell histology/predominant clear cell histology following prior cytokine therapy

9. Soft tissue sarcoma
9.1. Angiosarcoma
   Authorization of 3 months may be granted to members who are prescribed Avastin as a single agent.

9.2. Solitary fibrous tumor/hemangiopericytoma
Authorization of 3 months may be granted to members who are prescribed Avastin in combination with temozolomide.

10. Malignant pleural mesothelioma
Authorization of 3 months may be granted to members who are prescribed Avastin for the treatment of malignant pleural mesothelioma when criteria a. and b. below are met:
   a. Member has one of the following
      a. Unresectable or medically in operable clinical stage I to III disease with epithelial or mixed histology
      b. Clinical stage IV disease
      c. Tumor with sarcomatoid histology
   b. Avastin is used as a single agent for maintenance therapy or is used in combination with pemetrexed (Alimta) and cisplatin

11. Ophthalmic-related disorders
Authorization of 6 months may be granted to members who are prescribed Avastin for intravitreal injection for ANY of the following retinal disorders:
   a. Choroidal neovascularization (CNV) associated with high (pathologic) myopia, ocular histoplasmosis syndrome, angioid streaks, inflammatory conditions, or idiopathic
   b. Wet age-related macular degeneration (AMD) (including polypoidal choroidopathy and retinal angiomatosus proliferation subtypes of AMD)
   c. Macular edema due to retinal vein occlusion (RVO)
   d. Diabetic macular edema
   e. Ocular neovascularization (choroidal, retinal, iris) associated with proliferative diabetic retinopathy
   f. Neovascular glaucoma, as adjunct
   g. Retinopathy of prematurity
E. CONTINUATION OF THERAPY
   1. All approvable oncologic diagnoses (except CRC)
      Authorization of 3 months may be granted to members requesting authorization for continuation of
      therapy for all approvable oncologic diagnoses (except CRC) when ALL of the following criteria are
      met:
      a. Member has not had disease progression.
      b. Previous Avastin therapy was authorized by HMSA or member meets all initial criteria.

   2. Colorectal cancer
      Authorization of 3 months may be granted to members requesting authorization for continuation of
      therapy when Avastin is prescribed after first progression of unresectable advanced or metastatic
      disease and cancer progressed on a first-line Avastin-containing regimen as ONE of the following:
      a. In combination with FOLFIRI or irinotecan for members who were previously treated with an
         oxaliplatin-based regimen,
      b. In combination with FOLFOX or CapeOX for members who were previously treated with an
         irinotecan-based regimen, OR
      c. In combination with FOLFOX, CapeOX, irinotecan, irinotecan and oxaliplatin, or FOLFIRI for
         members who were treated with 5-FU with leucovorin or capecitabine regimen.

F. DOSAGE AND ADMINISTRATION
   Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted
   compendia, and/or evidence-based practice guidelines.

G. PROGRAM EXCEPTION – AKAMAI ADVANTAGE
   For Akamai Advantage members, the following National Coverage Determination (NCD) applies:
   • Anti-Cancer Chemotherapy for Colorectal Cancer (110.17).

H. ADMINISTRATIVE GUIDELINES
   Precertification is required. Please refer to the HMSA medical policy web site for the fax form.

IMPORTANT REMINDER
The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended
to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to
discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating
physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any
conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under
Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally
accepted standards of medical practice and review of medical literature and government approval
status. HMSA has determined that services not covered under this Medical Policy will not be medically
necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination
as to medical necessity in a given case, the physician may request that CVS/caremark reconsider the
application of the medical necessity criteria to the case at issue in light of any supporting
documentation.
REFERENCES


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Document History

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