Pharmacy Management Drug Policy

SUBJECT: Avastin (Bevacizumab)
POLICY NUMBER: PHARMACY-05
EFFECTIVE DATE: 9/2007
LAST REVIEW DATE: 5/1/2019

* This applies to outpatient as well as office-based administration *

If the member’s subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. Medical or drug policies apply to commercial and Health Care Reform products only when a contract benefit for the specific service exists.

DESCRIPTION:

Bevacizumab is a recombinant humanized monoclonal IgG1 antibody that binds to and inhibits the biologic activity of human vascular endothelial growth factor (VEGF). It prevents VEGF from stimulating blood vessel growth to the tumor.

Bevacizumab binds 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 results in reduction of microvascular growth and inhibition of metastatic disease progression.

POLICY:

Based upon our assessment and review of the peer-reviewed literature, Avastin has been medically proven to be effective and, therefore, medically appropriate for all FDA-approved indications and those indications which satisfy the Off-Label Use of FDA Approved Drugs policy. Due to the large range of acceptable uses for Avastin and because of the complex and fluid nature of the drug regimen recommendations employed in various clinical circumstances, a list of acceptable indications is not contained in this policy. Requests for Avastin use inconsistent with FDA labeling will be reviewed based on the Off-Label Use of FDA Approved Drugs policy.

I. Policy Guidelines:

A. Continuation of Avastin will not be authorized when disease progression has occurred on Avastin therapy and guidelines indicate therapy should be ceased.
   1. This does not apply to individuals with a diagnosis of colorectal cancer and evidence of progression while on a first-line Avastin-containing regimen. In these cases, continuation of Avastin will be allowed when used in combination with a different chemotherapy regimen.
   2. For cases of recurrent glioblastoma, please refer to National Comprehensive Cancer Network (NCCN) guidelines. In a case where a patient with good performance status (PS) who has received Avastin monotherapy shows signs of radiographic progression, continuation of Avastin therapy may prevent rapid neurologic deterioration, whereby approval may be medically appropriate.

B. Avastin therapy should not be initiated until at least 28 days following surgery and once wound healing has occurred. Discontinue Avastin at least 28 days prior to elective surgery.

C. Based upon assessment of peer-reviewed literature, Avastin, either as monotherapy or in combination with cytotoxic chemotherapy, is considered medically appropriate for use concurrent with alternating electrical field therapy (Tumor-Treatment Field (TTF))

D. **Dose** should not exceed 15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks.

E. The safety and effectiveness 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.

F. Unless otherwise stated above within the individual drug criteria, **approval time periods** are listed in the table below.

- Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy’s preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e.; generics, biosimilars, or other guideline-supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.

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II. **Bevacizumab (Avastin) is considered experimental and investigational for any of the following** indications because its effectiveness for these indications has not been established (not an all-inclusive list) and thus will not be covered: (please refer to Off-Label Use of FDA Approved Drugs policy)

1. Von Hippel Lindau disease
2. Sub-foveal neovascularization due to ocular histoplasmosis
3. Esophageal cancer
4. Pancreatic cancer
5. Prostate cancer
6. Cholangiocarcinoma
7. Mesothelioma
8. Melanoma
9. Multiple myeloma
10. Hepatocellular carcinoma
11. Hereditary Hemorrhagic Telangiectasia
Pharmacy Management Drug Policy
Avastin (Bevacizumab)

CODES:  Number

Description
Eligibility for reimbursement is based upon the benefits set forth in the member’s subscriber contract.
CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.
Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).

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HCPCS:  J9035,  Avastin
   C9257

UPDATES:

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REFERENCES:
- DrugDex and NCCN compendium accessed 5/1/2019
  4. Hochster HS, Hart LL, Ramanathan RK, et al. Safety and efficacy of oxaliplatin/fluoropyrimidine regimens with or without bevacizumab as first-line treatment of metastatic colorectal cancer (mCRC): Final analysis of the Tree 1 and 2 studies. 2006 ASCO [abstr 3510]


19. Chen H, Mooney M, Boron M et al: TRC-0301: bevacizumab (Avastin) plus 5-FU/leucovorin (FU/LV) for advanced colorectal cancer (CRC) that has progressed after standard chemotherapy. ASCO Annual Meeting 2004; [abstr 3315; oral presentation].
41. Robert NJ et al. RIBBON-1: Randomized, double-blind, placebo-controlled, phase III trial of chemotherapy with or without bevacizumab (B) for first-line treatment of HER2-negative locally recurrent or metastatic breast cancer (MBC). J Clin Oncol 27:15s, 2009
42. Miles D et al. Randomized, double-blind, placebo-controlled, phase III study of bevacizumab with docetaxel or docetaxel with placebo as first-line therapy for patients with locally recurrent or metastatic breast cancer (mBC): AVADO. J Clin Oncol 26: 2008