

**Blue Cross Blue Shield of Vermont and The Vermont Health Plan  
Prior Approval Guidelines  
Avastin™(bevacizumab)**

**Description:** Bevacizumab solution for IV infusion is a recombinant monoclonal IgG1 antibody that binds to vascular endothelial growth factor (VEGF) and inhibits its interaction with the Flt-1 and KDR receptors. This interaction normally leads to endothelial cell proliferation and the formation of new blood vessels.

Bevacizumab solution for Intravitreal administration is a recombinant monoclonal IgG1 antibody that binds to vascular endothelial growth factor (VEGF) and inhibits its interaction with the Flt-1 and KDR receptors. This interaction normally leads to endothelial cell proliferation and the formation of new blood vessels.

**Indications:** Bevacizumab is indicated as first line treatment in combination with 5-fluorouracil-based chemotherapy for metastatic carcinoma of the colon or rectum. Bevacizumab is indicated for first-line therapy in combination therapy with carboplatin and paclitaxel for the treatment of patients with unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer. Bevacizumab is indicated for the treatment of metastatic breast cell cancer and malignant glioma. Avastin® (bevacizumab), in combination with interferon-alfa, for the treatment of metastatic renal cell carcinoma.

Bevacizumab is not indicated for the treatment of neovascular (wet) age related macular degeneration. Bevacizumab is being used "off label" for the treatment of AMD based evidence from case study publications, open label clinical trials, and position statements from the AMD alliance which have demonstrated a beneficial impact on patients' vision. Bevacizumab is being widely employed for "off-label" use. There is ongoing research to determine the effectiveness of this agent for AMD.

**Warnings/  
Precautions:** Incidence of gastrointestinal perforation is about 2%, typically presenting as abdominal pain with constipation and vomiting. Wound dehiscence has also been reported. Discontinue treatment with bevacizumab if gastrointestinal perforation or wound dehiscence occurs. Patients with non-small cell lung cancer receiving bevacizumab with chemotherapy have experienced serious and sometimes fatal hemoptysis. Patients who have experienced recent hemoptysis should not receive bevacizumab. The most frequently reported adverse event was hypertension secondary to drug administration.

**Reasons for  
Prior  
Authorization:**  Cost                       Potential for misuse                       Toxicity

**Criteria for  
Approval:**

- 1) Diagnosis is an FDA-Labeled Indication **OR**
- 2) Diagnosis of neovascular (wet) age related macular degeneration.
- 3) Administration by a retinal expert.
- 4) The drug will be given monthly to the affected eye(s) at a dose of 1.25mg.
- 5) The patient understands the risks/benefits associated with the drug and has signed consent for acknowledging that the use of bevacizumab is "off-label" with unknown long term benefits.

**Reasons for  
Denial of  
Benefit:**

Oncology

- 1) Patient has had recent gastrointestinal surgery/perforation **OR** recent hemoptysis

Ophthalmology

- 2) The patient has an ocular or periocular infection.
- 3) The patient has uncontrolled hypertension.
- 4) The patient had not demonstrated improvement with therapy.
- 5) Patient does not meet criteria for Oncology or Ophthalmology

**Benefit  
Approval** Initial approval for 3 month period; Renewal approval period 6 months

**References:**

- 1) Avastin™ prescribing information, Genentech BioOncology, South San Francisco, CA, March 2008.
- 2) <http://www.amdalliance.org/information/treatments/treatment.php>
- 3) Lynch, S., Cheng, C. Bevacizumab for Neovascular Ocular Diseases
- 4) Bashshur, Z., Haddad, Z., Schakal, A. et al. Intravitreal Bevacizumab for Treatment of Neovascular Age-related Macular Degeneration: A One-year Prospective Study. Am J Ophthalmol 2008;145:249-256.