ROCKY MOUNTAIN HEALTH PLANS®
We understand Colorado. We understand you.

UNIFORM PHARMACY PRIOR AUTHORIZATION REQUEST FORM

CONTAINS CONFIDENTIAL PATIENT INFORMATION

Complete this form in its entirety and send to Rocky Mountain Health Plans at 858-357-2538

☐ **Urgent** [1] ☐ **Non-Urgent**

Requested Drug Name: Avastin® (bevacizumab)

Patient Information:	**Prescribing Provider Information:**
Patient Name:	Prescriber Name:
Member/Subscriber Number:	Prescriber Fax:
Policy/Group Number:	Prescriber Phone:
Patient Date of Birth (MM/DD/YYYY):	Prescriber Pager:
Patient Address:	Prescriber Address:
Patient Phone:	Prescriber Office Contact:
Patient Email Address:	Prescriber NPI:
	Prescriber DEA:
Prescription Date:	Prescriber Tax ID:
	Specialty/Facility Name (If applicable):
	Prescriber Email Address:

Prior Authorization Request for Drug Benefit: ☐ New Request ☐ Reauthorization

Patient Diagnosis and ICD Diagnostic Code(s):

Drug(s) Requested (with J-Code, if applicable):

Strength/Route/Frequency:

Unit/Volume of Named Drug(s):

Start Date and Length of Therapy:

Location of Treatment: (e.g. provider office, facility, home health, etc.) including name, Type 2 NPI (if applicable), address and tax ID:

Clinical Criteria for Approval, Including other Pertinent Information to Support the Request, other Medications Tried, Their Name(s), Duration, and Patient Response:

Avastin® (bevacizumab)

Diagnosis (documentation supportive of diagnosis is required)

☐ Metastatic colorectal cancer, 1st or 2nd line therapy, in combination with IV 5-fluorouracil-based chemotherapy

☐ Metastatic colorectal cancer, 2nd line therapy, in combination with fluoropyrimidine/irinotecan- or fluoropyrimidine/oxaliplatin-based chemotherapy, in patients who have progressed on a 1st line bevacizumab-containing regimen

☐ Non-squamous NSCLC (unresectable, locally advanced, recurrent, or metastatic)
☐ 1st line treatment in combination with carboplatin and paclitaxel

☐ Glioblastoma multiform of brain (recurrent, progressive disease) as a single agent following prior therapy
List prior therapy: _____

☐ Metastatic renal cell carcinoma in combination with interferon alfa

☐ Cervical cancer (recurrent, persistent, or metastatic) in combination with paclitaxel and cisplatin or paclitaxel and topotecan

☐ Platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan

☐ Patient has received no more than 2 prior chemotherapy regimens

☐ Other (please state): _____

For Ophthalmic conditions: See Coverage Policy

☐ For use in clinical trial? (If yes, provide trial name and registration number):

Drug Name (Brand Name and Scientific Name)/Strength:

Dose:	Route:	Frequency:
Quantity:	Number of Refills:	
Product will be delivered to: ☐ Patient's Home ☐ Physician Office		Other:
Prescriber or Authorized Signature:		Date:

Dispensing Pharmacy Name and Phone Number:

☐ **Approved** ☐ **Denied**

If denied, provide reason for denial, and include other potential alternative medications, if applicable, that are found in the formulary of the carrier:

1. A request for prior authorization that if determined in the time allowed for non-urgent requests could seriously jeopardize the life or health of the covered person or the ability of the covered person to regain maximum function, or subject the person to severe pain that cannot be adequately managed without the drug benefit contained in the prior authorization request

RMHP Formulary Coverage Policy

Avastin (bevacizumab)

THIS INFORMATION IS NOT ALL-INCLUSIVE AND IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY

CLASSIFICATION

Bevacizumab is a recombinant humanized monoclonal antibody directed against vascular endothelial growth factor (VEGF).

DESCRIPTION

- Avastin® (bevacizumab), a recombinant humanized monoclonal antibody, is an antineoplastic agent. The drug is an IgG1 antibody that contains human framework regions and murine complementarity-determining regions.
- Bevacizumab binds to human vascular endothelial growth factor (VEGF) and prevents interaction of VEGF with its receptors (Flt-1, KDR) on the surface of endothelial cells. In vitro models of angiogenesis have shown that interaction of VEGF with its receptors may lead to endothelial cell proliferation and new blood vessel formation. Evidence from animal models has suggested that administration of an anti-VEGF monoclonal antibody (e.g., bevacizumab) may inhibit angiogenesis and thus may reduce microvascular growth of tumors and inhibit metastatic disease progression. Bevacizumab is metabolized and eliminated via the reticuloendothelial system.
- VEGF is the major angiogenic stimulus responsible for the formation of choroidal neovascularization and so represents a new paradigm in the treatment of retinovascular disease. Given intraocularly, it has been investigated to treat a variety of conditions (e.g., age-related macular degeneration (ARMD), proliferative diabetic retinopathy, neovascular glaucoma, and the macular edema of vein occlusions).
- Bevacizumab (Avastin) is closely related to ranibizumab and appears to be a safe and effective treatment in the short term for AMD (Ziemssen et al.). It has been used off-label for many years for these patients. At about 1%-5% of the cost of ranibizumab, many clinicians believe that patients should be informed about this alternative, especially the significant price difference (Ziemssen et al.). The Comparison of the Age-related Macular Degeneration Treatment Trials (sponsored by the US National Eye Institute) is currently in progress. Some authors who have undergone smaller trials and systematic reviews believe that these two modalities will be shown to be equivalent in effect (Schouten et al.).
- On July 20, 2010, an advisory panel voted 12 to 1 to recommend that the FDA remove the advanced breast cancer indication from Avastin. The Oncologic Drugs Advisory Committee voted that bevacizumab, when added to standard chemotherapy, does not extend PFS long enough to be clinically meaningful in patients with HER2-negative, metastatic breast cancer.

FORMULARY COVERAGE

Prior authorization:	Required
Good Health Formulary:	Tier 6; Medical Benefit
Commercial Formulary:	Tier 6; Medical Benefit
Medicare Part D coverage:	Part B if administered incident to a physician’s service. Part D if obtained from any pharmacy.

COVERAGE CRITERIA

Cancer:

**Note: Supporting documentation from the patient's medical record is required for all cancer-related indications.*

RMHP considers bevacizumab (Avastin) **medically necessary** for any FDA approved indication, including the following:

1. Metastatic cancer of the colon or rectum in combination with 5-fluorouracil-based chemotherapy
2. Metastatic colorectal cancer, 2nd line therapy, in combination with fluoropyrimidine/irinotecan- or fluoropyrimidine/oxaliplatin-based chemotherapy, in patients who have progressed on a first-line bevacizumab-containing regimen.
3. Metastatic renal cell carcinoma in combination with interferon alfa
4. Non-squamous, non-small cell lung cancer that is recurrent or metastatic, unresectable, locally advanced, as first line treatment in combination with paclitaxel and carboplatin
5. Gliomas of the brain including anaplastic astrocytomas (grade 3) and glioblastoma multiforme (grade 4) (salvage therapy)

Ophthalmic:

Note: the following ophthalmic conditions **do not require a Prior Authorization.*

RMHP considers bevacizumab (Avastin) medically necessary administered as an intravitreal injection by an Ophthalmologist for the following*:

ICD-10	Description
H35.32	Exudative age-related macular degeneration
H35.351	Cystoid macular degeneration, right eye
H35.352	Cystoid macular degeneration, left eye
H35.353	Cystoid macular degeneration, bilateral
E08.311	Diabetes mellitus due to underlying condition with unspecified diabetic retinopathy with macular edema
E08.319	Diabetes mellitus due to underlying condition with unspecified diabetic retinopathy without macular edema
E08.321	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema
E08.329	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy without macular edema
E08.331	DM due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema
E08.339	DM due to underlying condition with moderate nonproliferative diabetic retinopathy without macular edema
E08.341	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema
E08.349	DM due to underlying condition with severe nonproliferative diabetic retinopathy without macular edema
E08.351	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema
E08.359	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy without macular edema
E09.311	Drug or chemical induced diabetes mellitus with unspecified diabetic retinopathy with macular edema
E09.319	Drug or chemical induced diabetes mellitus with unspecified diabetic retinopathy without macular edema
E09.321	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema
E09.329	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema
E09.331	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
E09.339	Drug or chemical induced DM with moderate nonproliferative diabetic retinopathy without macular edema
E09.341	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
E09.349	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema
E09.351	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema
E09.359	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy without macular edema
E10.311	Type 1 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E10.319	Type 1 diabetes mellitus with unspecified diabetic retinopathy without macular edema
E10.321	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema

E10.329	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema
E10.331	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
E10.339	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema
E10.341	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
E10.349	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema
E10.351	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema
E10.359	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema
E11.311	Type 2 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E11.319	Type 2 diabetes mellitus with unspecified diabetic retinopathy without macular edema
E11.321	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema
E11.329	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema
E11.331	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
E11.339	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema
E11.341	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
E11.349	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema
E13.351	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema
E13.359	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema
H21.1X1	Other vascular disorders of iris and ciliary body, right eye
H21.1X2	Other vascular disorders of iris and ciliary body, left eye
H21.1X3	Other vascular disorders of iris and ciliary body, bilateral
H34.811	Central retinal vein occlusion, right eye
H34.812	Central retinal vein occlusion, left eye
H34.813	Central retinal vein occlusion, bilateral
H34.831	Tributary (branch) retinal vein occlusion, right eye
H34.832	Tributary (branch) retinal vein occlusion, left eye
H34.833	Tributary (branch) retinal vein occlusion, bilateral
H34.9	Unspecified retinal vascular occlusion
H35.051*	Retinal neovascularization, unspecified, right eye
H35.052*	Retinal neovascularization, unspecified, left eye
H35.053*	Retinal neovascularization, unspecified, bilateral
H35.071	Retinal telangiectasis, right eye
H35.072	Retinal telangiectasis, left eye
H35.073	Retinal telangiectasis, bilateral
H35.20	Other non-diabetic proliferative retinopathy, unspecified eye
H35.21	Other non-diabetic proliferative retinopathy, right eye
H35.22	Other non-diabetic proliferative retinopathy, left eye
H35.23	Other non-diabetic proliferative retinopathy, bilateral
H35.81	Retinal edema
H35.82	Retinal ischemia
H40.89	Other specified glaucoma
H44.20	Degenerative myopia, unspecified eye
H44.21	Degenerative myopia, right eye
H44.22	Degenerative myopia, left eye
H44.23	Degenerative myopia, bilateral

*codes subject to change based on Medicare coverage determination changes

Background:

- Avastin (bevacizumab) is not FDA approved for these ophthalmic conditions, including age related (wet) macular degeneration
- Intravitreal administration of Avastin (bevacizumab) is a CMS Compendia supported use for a variety of ophthalmic disorders
- Avastin (bevacizumab) is a recombinant humanized monoclonal IgG1 antibody that is similar to Lucentis (ranibizumab), a drug developed expressly for intravitreal use
- Avastin (bevacizumab) is widely used by ophthalmologists and the American Academy of Ophthalmology supports treating age-related macular degeneration (AMD) with intravitreal injections of bevacizumab to meet the medical needs of many patients who have not responded to therapy with ocular photodynamic therapy (OPT) with verteporfin or intravitreal pegaptanib

- Intravitreal Avastin (bevacizumab) is prepared by compounding pharmacies and costs under $100 per eye. Lucentis (ranibizumab) cost is well over $2,000 per eye per treatment.
- Avastin (bevacizumab) is formulated for intravenous infusion, not intravitreal injection, thus although Avastin is similar to Lucentis, they differ in some respects:
  - The Avastin molecule is larger than Lucentis (149kD vs. 48kD). This may impact penetration into the layers of the retina, but the clinical implications are unknown
  - Avastin has a longer half-life than Lucentis (20 days compared to 4 hours) that may allow for less frequent administration
  - Lucentis doesn't have Fc portion in this antibody fragment, which may cause less inflammation within the eye.

RMHP considers the use of Avastin (bevacizumab) to be **experimental** for the following:
- Any condition or diagnosis not FDA approved or Compendia supported.
- Any ophthalmic ICD-10 code not listed as medically necessary

Required Provider Specialty:
- Approval is limited to Oncology and Ophthalmology

DOSAGE/ADMINISTRATION:

Intravenous route
- **Glioblastoma multiforme of brain:** The recommended dose of bevacizumab for patients with progressive glioblastoma following prior therapy is 10 mg/kg IV over 90 minutes once every 2 weeks until disease progression or unacceptable toxicity. If the previous infusion is tolerated, bevacizumab may be administered over 60 minutes on the second infusion and 30 minutes on all subsequent infusions.
- **Metastatic colorectal cancer, first- or second-line therapy, in combination with IV 5-fluorouracil-based chemotherapy:**
  - First-line therapy: Bevacizumab 5 mg/kg given IV over 30 to 90 minutes day 1, in combination with FOLFOX-4 (oxaliplatin + leucovorin followed by a bolus and infusional 5-fluorouracil), every 2 weeks was studied as first-line treatment for metastatic colorectal cancer in a randomized, placebo-controlled, phase 3 trial. The FOLFOX-4 regimen was given every 2 weeks as follows: leucovorin (LV) 200 mg/m(2) IV over 2 hours followed by a 5-fluorouracil (5-FU) 400 mg/m(2) IV bolus followed by a 5-FU 600 mg/m(2) 22-hr continuous IV infusion days 1 and 2 plus oxaliplatin 85 mg/m(2) IV over 2 hours (given concurrently with LV) on day 1 only.
  - First-line therapy: In patients with metastatic carcinoma of the colon or rectum, the recommended dose of bevacizumab in combination with bolus-IFL (irinotecan, 5-fluorouracil, leucovorin) is 5 mg/kg IV once every 2 weeks until disease progression or unacceptable toxicity. Bevacizumab is initially infused over 90 minutes; however, if the 90 minute infusion is tolerated, decrease the infusion time to 60 minutes for the second infusion and 30 minutes for all subsequent infusions [41]. The bolus-IFL regimen was as follows: irinotecan 125 mg/m(2) IV, 5-fluorouracil 500 mg/m(2) IV, and leucovorin 20 mg/m(2) IV once weekly for 4 weeks on and 2 weeks off.
  - Second-line therapy: In patients with metastatic carcinoma of the colon or rectum, the manufacturer recommended dose of bevacizumab in combination with FOLFOX-4 (oxaliplatin + leucovorin followed by a bolus and infusional 5-fluorouracil), is 10 mg/kg IV once every 2 weeks until disease progression or unacceptable toxicity. Bevacizumab is initially infused over 90 minutes; however, if the 90 minute infusion is tolerated, decrease the infusion time to 60 minutes for the second infusion and 30 minutes for all subsequent infusions. This bevacizumab

dose, in combination with FOLFOX-4, was studied as second-line therapy for patients with metastatic colorectal cancer in a multicenter, open-label, randomized clinical trial. The FOLFOX-4 regimen was given every 2 weeks as follows: leucovorin (LV) 200 mg/m(2) IV over 2 hours followed by a 5-fluorouracil (5-FU) 400 mg/m(2) IV bolus followed by a 5-FU 600 mg/m(2) 22-hour continuous IV infusion days 1 and 2 plus oxaliplatin 85 mg/m(2) IV over 2 hours (given concurrently with LV) on day 1 only.

- **Metastatic colorectal cancer, second-line therapy, in combination with fluoropyrimidine/irinotecan- or fluoropyrimidine/oxaliplatin-based chemotherapy, in patients who have progressed on a first-line bevacizumab-containing regimen:**
  - The recommended dose of bevacizumab in combination with fluoropyrimidine/irinotecan- or fluoropyrimidine/oxaliplatin-based chemotherapy is 5 mg/kg IV every 2 weeks or 7.5 mg/kg IV every 3 weeks. Bevacizumab is initially infused over 90 minutes; however, if the 90 minute infusion is tolerated, decrease the infusion time to 60 minutes for the second infusion and 30 minutes for all subsequent infusions. Continue treatment until disease progression or unacceptable toxicity
- **Metastatic colorectal cancer, first-line therapy, in combination with oxaliplatin and capecitabine (XELOX):**
  - Bevacizumab 7.5 mg/kg given IV over 30 - 90 minutes day 1, in combination with XELOX (oxaliplatin + capecitabine), every 3 weeks was studied as first-line treatment for metastatic colorectal cancer in a randomized, placebo-controlled, phase 3 trial. The XELOX regimen was given every 3 weeks as follows: oxaliplatin 130 mg/m(2) IV over 2 hours day 1 followed by capecitabine 1000 mg/m(2) twice daily days 1 to 14.
- **Metastatic renal cell carcinoma, in combination with interferon alfa:**
  - The recommended dose of bevacizumab in the treatment of metastatic renal cell carcinoma is 10 mg/kg IV once every 2 weeks in combination with interferon alfa until disease progression or unacceptable toxicity. In clinical trials interferon alfa-2a or alfa-2b was dosed at 9 million international units subcutaneously 3 times per week for a maximum of 52 weeks. Bevacizumab is initially infused over 90 minutes; however, if the 90 minute infusion is tolerated, decrease the infusion time to 60 minutes for the second infusion and 30 minutes for all subsequent infusions.
- **Non-small cell lung cancer:**
  - For the first-line treatment of unresectable, locally advanced, recurrent or metastatic nonsquamous, non-small cell lung cancer, the recommended dosage of bevacizumab is 15 mg/kg IV over 90 minutes once every 3 weeks in combination with carboplatin and paclitaxel until disease progression or unacceptable toxicity. If the first infusion is tolerated, bevacizumab may be administered over 60 minutes on the second infusion and 30 minutes on all subsequent infusions. Six cycles of bevacizumab 15 mg/kg IV in combination with paclitaxel 200 mg/m(2) IV and carboplatin (target AUC 6) IV on day 1 once every 3 weeks has been used in clinical trials. After 3 to 6 cycles of combination therapy, single-agent bevacizumab was continued until disease progression or intolerable toxicity in some patients.

Intravitreal route

- Age related macular degeneration, Secondary to choroidal neovascularization (off-label use):
  - Study dose: 1.25 mg via intravitreal injection once every 4 weeks, 6 weeks, or 8 weeks continuously for 1 year, regardless of visual acuity change.
  - Study Dose: 1.25 mg via intravitreal injection once monthly for a total of 3 injections or until macular edema, subretinal fluid and/or pigment epithelial detachment resolved.
  - Study Dose: 2.5 mg via intravitreal injection every 4 weeks for a total of 3 injections.
- Branch retinal vein occlusion with macular edema (off-label use):

- Study dose: 1.25 mg via intravitreal injection 1 time, repeated at 1 to 3 month intervals if the foveal thickness was 250 mcm or greater, or if there was persistent or recurrent macular edema (mean of 3.8 injections over 2 years).
- Central retinal vein occlusion with macular edema (off-label use)
  - Study dose: 1.25 mg (0.05 mL) intravitreal injection every 6 weeks for 24 weeks (4 injections)
- Diabetic macular edema (off-label use)
  - Study dose: 1.25 mg intravitreal injection at baseline and at 6 and 12 weeks

PRECAUTIONS:

- Black Box Warnings for IV Solution:
  - Gastrointestinal Perforations: The incidence of gastrointestinal perforation, some fatal, in bevacizumab-treated patients ranges from 0.3 to 2.4%. Discontinue bevacizumab in patients with gastrointestinal perforation.
  - Surgery and Wound Healing Complications: The incidence of wound healing and surgical complications, including serious and fatal complications, is increased in bevacizumab-treated patients. Discontinue bevacizumab in patients with wound dehiscence. The appropriate interval between termination of bevacizumab and subsequent elective surgery required to reduce the risks of impaired wound healing/wound dehiscence has not been determined. Discontinue at least 28 days prior to elective surgery. Do not initiate bevacizumab for at least 28 days after surgery and until the surgical wound is fully healed.
  - Hemorrhage: Severe or fatal hemorrhage, including hemoptysis, gastrointestinal bleeding, central nervous systems (CNS) hemorrhage, epistaxis, and vaginal bleeding occurred up to five-fold more frequently in patients receiving bevacizumab. Do not administer bevacizumab to patients with serious hemorrhage or recent hemoptysis
- Do not administer bevacizumab to patients with recent hemoptysis (0.5 teaspoon or more of red blood) due to increased risk of potentially fatal hemorrhage.
- Temporarily suspend bevacizumab in the following conditions: moderate to severe proteinuria, hypertension (severe, not controlled), and surgery.
- Elective surgery due to risk of impaired wound healing/wound dehiscence. Discontinue use at least 28 days prior to elective surgery and do not reinitiate therapy for at least 28 days following surgery and until surgical wound is fully healed.
- Gastrointestinal (GI) perforation, intra-abdominal abscess, and fistula formation (e.g., gastrointestinal, enterocutaneous, esophageal, duodenal, rectal), some cases fatal, have been reported. Discontinue therapy for GI perforation, abscess, or fistula.
- Hemorrhage (e.g., intracranial, gastrointestinal, pulmonary, vaginal), some cases serious and requiring medical management or resulting in fatality, has been reported. Discontinue therapy for serious hemorrhage.
- Wound dehiscence and wound healing complications, some cases fatal, have occurred. Discontinue therapy if wound dehiscence occurs.
- Arterial thromboembolic events (ATE) (e.g., cerebral infarction, transient ischemic attacks, myocardial infarction, angina), some cases fatal, have occurred; increased risk with concomitant chemotherapy in diabetic patients, those older than 65 years of age, or a history of arterial thromboembolism; discontinue therapy for severe ATE.
- Colon cancer, adjuvant, in combination with chemotherapy (unapproved use); lack of efficacy and not indicated.
- Elderly (65 years or older) have increased risk of developing serious adverse events.

- Nongastrointestinal fistula formation (e.g., tracheo-esophageal, bronchopleural, biliary, vaginal, renal, and bladder), some cases fatal, has occurred. Discontinue therapy for fistula formation of an internal organ.
- Hypertension (grade 3 or 4) has been reported; monitoring is recommended. Temporarily withhold therapy for severe hypertension not controlled with medical management. Discontinue therapy for hypertensive crisis or hypertensive encephalopathy.
- Infusion reactions (e.g., hypertension, hypertensive crises with neurologic signs and symptoms, wheezing, oxygen desaturation, grade 3 hypersensitivity, chest pain, headache, rigors, and diaphoresis) have been reported. Discontinue therapy for severe infusion reactions.
- Necrotizing fasciitis, some cases fatal, has been reported. Usually reported secondary to wound healing complications, gastrointestinal perforation, or fistula formation. Discontinue use if necrotizing fasciitis occurs.
- Nephrotic syndrome, some cases fatal, has been reported. Discontinue therapy if nephrotic syndrome occurs.
- Ovarian failure, which may impair fertility, has been reported, especially in premenopausal women receiving bevacizumab in combination with mFOLFOX chemotherapy for adjuvant treatment of colorectal cancer (unapproved use).
- Monitor for proteinuria. Withhold therapy for 2 g proteinuria or greater per 24 hours.
- Reversible posterior leukoencephalopathy syndrome (RPLS) has occurred from 16 hours to 1 year following initiation of therapy. Discontinue therapy if RPLS occurs.

Billing/Coding information

HCPCS Code:

J9035	Injection, bevacizumab, 10mg
C9257	Injection, bevacizumab, 0.25mg

Associated CPT Coding:

67028	Intravitreal injection of a pharmacologic agent
96401 & 96417	Chemotherapy administration, subcutaneous or intramuscular; non-hormonal anti-neoplastic
92134	Scanning computerized ophthalmic diagnostic imaging, posterior segment, with interpretation and report, unilateral or bilateral, retina

COST

AWP (March 2010)
- 100 mg / 4 ml: $669.90
- 400 mg / 16 ml: $2,679.60
- Preparation for intravitreal injection (non-licensed): <$100 per treated eye per month
    - Lucentis (AWP, April 2010): 0.5mg/0.05ml injection: $2,437.50 per treated eye per month

AWP (March 2012)
- 100 mg/ 4 ml: $599.30
- 400 mg/16 ml: $2,397.20
    - Lucentis (AWP, March 2012): 0.5mg/0.05ml injection: $1,971.25 per treated eye per month

COMMITTEE APPROVAL:

- March 2004
- May 2006 - Macular degeneration

GUIDELINE UPDATE INFORMATION:

3/25/2010	Initial policy creation
March 2012	Coverage Policy updated
August 2015	Coverage Policy updated
October 2015	ICD-10 codes added to Coverage Policy

REFERENCES:

- DRUGDEX®, accessed 03/29/2010, 03/06/2012, 8/25/2015
- Product Information: AVASTIN® IV infusion, bevacizumab IV infusion. Genentech, Inc, South San Francisco, CA, 2015.
- Schouten et al. A systematic review on the effect of bevacizumab in exudative age-related macular degeneration. Graefes Arch Clin Exp Ophthalmol. 2009: 247: 1-11.
- Ziemssen et al. Off-Label Use of Bevacizumab for the Treatment of Age-Related Macular Degeneration- What is the Evidence? Drugs Aging. 2009; 26(4): 295-314.
- Intraocular bevacizumab coding/billing guidelines. Noridian Healthcare Solutions. Available at: https://med.noridianmedicare.com/web/jfb/policies/coverage-articles/intraocular-bevacizumab-coding-billing-guidelines