Health Net®

Prior Authorization Protocol

AVASTIN® (bevacizumab)

NATL

Coverage of drugs is first determined by the member's pharmacy or medical benefit. Please consult with or refer to the Evidence of Coverage document.

I. FDA Approved Indications:

- Metastatic colorectal cancer, with intravenous 5-fluorouracil-based (5-FU) chemotherapy for first- or second-line treatment.
- Metastatic colorectal cancer, 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, with carboplatin and paclitaxel for the 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.
  -Effectiveness based on improvement in objective response rate. No data available demonstrating improvement in disease-related symptoms or survival with Avastin.
- Metastatic renal cell carcinoma with interferon alpha
- Cervical cancer, in combination with paclitaxel and cisplatin or paclitaxel and topotecan in persistent, recurrent, or metastatic disease.
- For treatment of platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, in combination with paclitaxel, pegylated liposomal doxorubin or topotecan.

II. Health Net Approved Indications and Usage Guidelines:

Approve for any of the following:

- Diagnosis of Neovascular (Wet) Age-Related Macular Degeneration confirmed by an ophthalmologist
- Diagnosis of Neovascular Glaucoma and failure of maximal doses of one approved antiglaucoma medication.
- Diagnosis of proliferative diabetic retinopathy and patient will be undergoing vitrectomy
- Diagnosis of macular edema secondary to retinal vein occlusion
- Diagnosis of diabetic macular edema
- Diagnosis of metastatic carcinoma of the colon or rectum and used in combination with a 5-fluorouracil-based chemotherapy regimen
- Diagnosis of metastatic carcinoma of the colon or rectum in patients whose disease has progressed following an Avastin containing regimen and used in combination with fluoropyrimidine- irinotecan- or fluoropyrimidine-oxaliplatin chemotherapy regimen
- Diagnosis of non-squamous, non-small cell lung carcinoma (NSCLC) and used in combination with platinum-based systemic chemotherapy (e.g. cisplatin, carboplatin) and paclitaxel

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- Diagnosis of ovarian cancer and failure or clinically significant adverse effects to two chemotherapy regimens
- Diagnosis of relapsed or medically unresectable stage IV renal carcinoma and used in combination with interferon alfa-2a
- Recurrence or salvage therapy of Glioblastoma Multiforme, Anaplastic Astrocytoma or Anaplastic Oligoendroglioma as a single agent or in combination with irinotecan, carmustine, lomustine, temozolomide, or carboplatin
- Diagnosis of soft tissue sarcoma

  AND

  - Angiosarcoma

  OR

  - Solitary fibrous tumor/hemangiopericytoma
- Diagnosis of persistent, recurrent, or metastatic cervical cancer and used in combination with paclitaxel and cisplatin or paclitaxel and topotecan
- Diagnosis of platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, in combination with paclitaxel, pegylated liposomal doxorubin or topotecan.

III. Coverage is Not Authorized For:

- Metastatic carcinoma of the colon or rectum: use as a single agent. Avastin as a single agent resulted in inferior survival rates when compared to FOLFOX regimen.
- NSCLC: patients with squamous histology due to increased risk of hemoptysis.
- The addition of Avastin to gemcitabine as first-line therapy for carcinoma of the pancreas did not improve survival in advanced pancreatic cancer in comparison to gemcitabine given alone.
- Avastin monotherapy for use in hormone refractory prostate cancer was shown to be relatively ineffective in a small study of fifteen patients. The McGill Present Pain Index indicated a trend toward increasing pain during the study.
- Non-FDA approved indications, which are not listed in the Health Net Approved Indications and Usage Guidelines section unless there is sufficient documentation of efficacy and safety in the published literature.

IV. General Information:

- The FDA revoked the approval of the breast cancer indication for Avastin (bevacizumab) on November 18, 2011. Avastin used for metastatic breast cancer has not been shown to provide a benefit, in terms of delay in the growth of tumors, that would justify its serious and potentially life-threatening risks. Nor is there evidence that use of Avastin will either help women with breast cancer live longer or improve their quality of life. More information at: http://www.fda.gov/NewsEvents/Newsroom/ucm279485.htm

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- Fatal pulmonary hemorrhage can occur in patients with NSCLC treated with chemotherapy and Avastin. The incidence of severe or fatal hemoptysis was 31% in patients with squamous histology and 2.3% with NSCLC excluding predominant squamous histology. Patients with recent hemoptysis should not receive Avastin.
- Avastin has been added to the National Comprehensive Cancer Network (NCCN) practice guidelines as category 2A for recurrent ovarian cancer for patients who have progressed on two consecutive single-agent regimens without evidence of clinical benefit.
- Age-related macular degeneration, secondary to choroidal neovascularization
    - In a prospective time-series trial, bevacizumab 2.5 mg was administered by intravitreal injection every 4 weeks for a total of 3 injections
    - In one retrospective study, bevacizumab 1.25 mg was administered by intravitreal injection once monthly for a total of three injections.
    - In another retrospective study intravitreal bevacizumab 1.25 mg was administered once monthly until macular edema, subretinal fluid and/or pigment epithelial detachment resolved (Avery et al, 2006).
- Avastin, with or without irinotecan, has been added to the NCCN practice guidelines for recurrent or salvage therapy of Glioblastoma Multiforme and Anaplastic Astrocytoma, but is considered 2B in combination with carboplatin.
- Avastin is effective for the treatment of neovascular glaucoma that is not responsive to maximal doses of antiglaucoma medications. While most studies did not indicate the agents that were tried and failed prior to the use of Avastin in neovascular glaucoma, one study did indicate the use of timolol, dorzolamide and brimonidine before an Avastin injection.
- Avastin is category 2A for the treatment of soft tissue sarcoma-angiosarcoma and soft tissue sarcoma-solitary fibrous tumor/hemangiopericytoma in the NCCN practice guidelines for soft tissue sarcomas.
- Avastin is a category 2A ,in the NCCN practice guidelines, for the treatment of adult intracranial and spinal ependymoma (excluding subependymoma).
- Avastin is category 2A, in the NCCN practice guidelines, for the treatment of non-clear cell renal carcinoma.
- Avastin is category 2A, in the NCCN practice guidelines, for the treatment of endometrial carcinoma
- Avastin in combination with cisplatin/paclitaxel has been added to the NCCN practice guidelines as category 1 for recurrent or metastatic cervical cancer. Avastin in combination with topotecan/paclitaxel has been added as a category 2B recommendation for this same indication.
- Avastin is rated category 2A, in the NCCN practice guidelines, for the diagnosis of relapsed or medically unresectable stage IV renal carcinoma following prior cytokine therapy (a rating of 2B is given if following prior tyrosine kinase inhibitor therapy).
- Avastin has a black box warning for gastrointestinal perforation, surgery and wound healing complications, and hemorrhage. Avastin should be discontinued in patients with wound dehiscence. Discontinue at least 28 days prior to elective surgery. Do not initiate Avastin for at least 28 days after surgery and until the surgery wound is fully healed. Avastin causes severe or fatal hemorrhage, hemoptysis, gastrointestinal bleeding, CNS hemorrhage, and vaginal bleeding. Do not administer to patients with serious hemorrhage or recent

hemoptysis.

V. Therapeutic Alternatives:

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
Metastatic carcinoma of the colon or rectum		
FOLFOX4 = Infusional 5-FU/leucovorin/ oxaliplatin	Oxaliplatin 85 mg/m^2 IV over 2 hours day 1; leucovorin 200 mg/m^2 IV over 2 hours days 1 & 2, followed by 5-FU 400 mg/m^2 IV bolus over 2-4 minutes, followed by 600 mg/m^2 IV 5-FU continuous infusion over 22 hours on days 1 & 2. Repeat cycle every 14 days.	
FOLFIRI = Infusional 5-FU/ leucovorin/Camptosar® (irinotecan)	Camptosar 180 mg/m^2 IV over 90 minutes day 1; Leucovorin 400 mg/m^2 IV over 2 hours day 1 followed by 5-FU 400 mg/m^2 IV bolus over 2-4 minutes, followed by 2.4 gm/m^2 IV 5-FU continuous infusion over 46 hours. Repeat cycle every 14 days.	
Capecitabine (Xeloda)	2500 mg/m^2 PO daily divided Q12h for 2 weeks; repeat cycles of 2 weeks on and 1 week off. For patients who cannot tolerate intensive therapy.	
NSCLC		
Cisplatin Carboplatin Paclitaxel Docetaxel Vinorelbine Gemcitabine Etoposide Irinotecan Vinblastine Mitomycin Ifosfamide Alimta (pemetrexed disodium) (2nd line)	Various doses	Number of cycles varies
Ovarian Cancer		
Carboplatin and Paclitaxel	Carboplatin dosed at an area under the curve (AUC) of 5-7.5 and paclitaxel 175 mg/m^2 IV over 3 hours given every 3 weeks for 6 courses.	
Docetaxel Taxotere and Carboplatin	Docetaxel, 60-75 mg/m^2 IV over 1 hour plus carboplatin dosed at AUC of 5 to 6 every 3 weeks.	
Glioblastoma Multiforme		
Temodar® (temozolomide)	Maintenance phase cycles: 150 mg-200 mg/m² PO days 1-5. Repeat every 28 days.	

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Drug	Dosing Regimen	Dose Limit/ Maximum Dose
BICNU® (carmustine)	150 mg-200 mg/m² IV day 1. Repeat every 6-8 weeks for one year or tumor progression.	
Cervical Cancer		
cisplatin/paclitaxel	Paclitaxel: I.V.: 135 mg/m^2 continuous infusion over 24 hours day 1 Cisplatin: I.V.: 50 mg/m^2 day 2 Repeat cycle every 21 days for up to a total of 6 cycles; responders may continue beyond 6 cycles	
cisplatin/topotecan (Hycamtin)	Topotecan: I.V.: 0.75 mg/m^2/day days 1, 2, and 3 Cisplatin: I.V.: 50 mg/m^2 day 1 only Repeat cycle every 21 days for up to a total of 6 cycles; responders may continue beyond 6 cycles	
Topotecan (Hycamtin)/paclitaxel	Paclitaxel: I.V.: 135 mg/m^2 continuous infusion over 24 hours day 1 Topotecan: I.V.: 0.75 mg/m^2/day days 1, 2, and 3 Repeat cycle every 21 days for up to a total of 6 cycles; responders may continue beyond 6 cycles	

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VI. Recommended Dosing Regimen and Authorization Limit:

Drug	Dosing Regimen	Authorization Limit

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Drug	Dosing Regimen	Authorization Limit
Avastin	Colorectal Cancer: 5 mg/kg or 10 mg/kg once every 14 days as an IV infusion in combination with a 5-FU based chemotherapy regimen until disease progression is detected. 5 mg/kg every 2 weeks or 7.5 mg/kg every 3 weeks when used in combination with a fluoropyrimidine-irinotecan or fluoropyrimidine-oxaliplatin based chemotherapy regimen in patients who have progressed on a first-line Avastin-containing regimen Non-Squamous, Non-Small Cell Lung Cancer: 15 mg/kg IV infusion every 3 weeks with carboplatin/paclitaxel Ovarian Cancer: 15 mg/kg IV infusion every 3 weeks Platinum resistant ovarian cancer: 10 mg/kg intravenously every 2 weeks with weekly paclitaxel, liposomal doxorubicin, or topotecan or 15mg/kg every 3 weeks if given with topotecan every 3 weeks. Clear cell renal carcinoma: 10 mg/kg IV every 2 weeks with interferon alfa Glioblastoma Multiforme, Anaplastic Astrocytoma, Anaplastic Oligodendroglioma:10 mg/kg IV every 2 weeks Soft tissue sarcoma: 15 mg/kg IV infusion every 3 weeks Cervical Cancer: 15 mg/kg IV infusion every 3 weeks (in combination with paclitaxel and either cisplatin or topotecan) until disease progression or unacceptable toxicity	Length of benefit
	Neovascular (Wet) Macular Degeneration: 1.25 to 2.5 mg administered by intravitreal injection every 4 weeks	Length of benefit
	Neovascular Glaucoma: 1.25 mg administered by intravitreal injection every 4 weeks	Length of benefit
	Macular edema secondary to retinal vein occlusion: 1 mg to 2.5 mg administered by intravitreal injection every 4 weeks	Length of benefit
	Proliferative diabetic retinopathy: 1.25 mg administer by intravitreal injection 5 to 20 days before vitrectomy	Length of benefit
	Diabetic Macular Edema: 1.25 mg administered by intravitreal injection	Length of benefit

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VII. Product Availability:

Single use vials: 100 mg/4 ml, 400 mg/16 ml

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