

Market Applicability							
Market	DC	GA	KY	MD	NJ	NY	WA
Applicable	X	X	X	X	X	X	X

Bevacizumab Agents (Avastin, Mvasi)

Override(s)	Approval Duration
Prior Authorization	1 year

Medications
Avastin (bevacizumab) Mvasi (bevacizumab-awwb)

APPROVAL CRITERIA

Requests for bevacizumab (Avastin, Mvasi) may be approved if the following criteria are met:

- I. Individual has a diagnosis of one of the following:
 - A. Diabetic macular edema (AAO 2017); **OR**
 - B. Proliferative diabetic retinopathy with or without diabetic macular edema (DP B IIa); **OR**
 - C. Established neovascular “wet” age-related macular degeneration (AHFS); **OR**
 - D. Macular edema from branch retinal vein occlusion (AAO 2015); **OR**
 - E. Macular edema from central retinal vein occlusion (AAO 2015); **OR**
 - F. Neovascular glaucoma (Costagliola 2008, DP B IIb); **OR**
 - G. Choroidal neovascularization associated with myopic degeneration (AAO Consensus 2017, DP B IIb); **OR**
 - H. Other rare causes of choroidal neovascularization for **one or more** of the following conditions (Weber 2016):
 1. angioid streaks; **OR**
 2. choroiditis (including, but not limited to histoplasmosis induced choroiditis); **OR**
 3. retinal dystrophies; **OR**
 4. trauma; **OR**
 5. pseudoxanthoma elasticum; **OR**
 - I. Radiation retinopathy (Finger 2016); **OR**
 - J. Retinopathy of prematurity (Sanker 2018, DP B IIb);

OR

- II. Individual has a diagnosis of metastatic Breast Cancer and the following are met (NCCN 2A):

This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply.

Market Applicability							
Market	DC	GA	KY	MD	NJ	NY	WA
Applicable	X	X	X	X	X	X	X

- A. Individual has HER2-negative breast cancer; **AND**
- B. Bevacizumab is used as first-line chemotherapy*; **AND**
- C. Bevacizumab is used in combination with paclitaxel or paclitaxel protein-bound;

*Note: Hormonal therapy alone is not considered “chemotherapy.”

OR

III. Individual has a diagnosis of Central Nervous System – Primary Tumor and the following are met:

- A. Individual has failed radiation therapy; **AND**
- B. Bevacizumab is used in a single line of therapy; **AND**
- C. The tumor to be treated is a World Health Organization (WHO) Grade III/IV glioma which includes but is not limited to:
 1. Anaplastic astrocytoma; **OR**
 2. Anaplastic glioma; **OR**
 3. Ependymoma, progressive or recurrent; **OR**
 4. Glioblastoma; **OR**
 5. Glioblastoma multiforme; **OR**
 6. High-grade glioma, recurrent;

OR

IV. Individual is using bevacizumab to treat symptomatic post-radiation necrosis of the central nervous system (NCCN 2A);

OR

V. Individual has a diagnosis of metastatic colon, rectal, or colorectal, small bowel, appendiceal, or anal adenocarcinoma and the following are met (Label, NCCN 2A):

- A. Bevacizumab is used in combination with 5-fluorouracil-based chemotherapy, irinotecan or oxaliplatin; **AND**
- B. Individual has not progressed on more than two lines of a bevacizumab-containing chemotherapy regimen (Simkens 2015);

OR

VI. Individual has a diagnosis of Vulvar Cancer and the following are met (NCCN 2A):

- A. Individual has advanced, recurrent or metastatic disease; **AND**
- B. Bevacizumab is used in combination with paclitaxel and cisplatin or carboplatin; **AND**
- C. Bevacizumab is used in a single line of therapy;

OR

VII. Individual has a diagnosis of Cervical Cancer and the following are met:

Market Applicability							
Market	DC	GA	KY	MD	NJ	NY	WA
Applicable	X	X	X	X	X	X	X

- A. Individual has persistent, recurrent, or metastatic disease that is not amenable to curative treatment with surgery or radiotherapy (Tewari 2014); **AND**
- B. Bevacizumab is being used in combination with paclitaxel and either topotecan, cisplatin, or carboplatin; **AND**
- C. Bevacizumab is used in a single line of therapy;

OR

VIII. Individual has a diagnosis of Endometrial Carcinoma and the following are met (NCCN 2A):

- A. Individual has advanced or recurrent disease; **AND**
 - 1. Bevacizumab is being used in combination with carboplatin and paclitaxel; **OR**
 - 2. Following combination therapy with carboplatin and paclitaxel, bevacizumab is being used as single-agent maintenance therapy until disease progression or prohibitive toxicity;

OR

IX. Individual has a diagnosis of Malignant Mesothelioma and the following are met (NCCN 2A):

- A. Bevacizumab is used as first-line therapy for unresectable disease when:
 - 1. Used in a first-line combination chemotherapy with pemetrexed and either cisplatin or carboplatin; **AND**
 - 2. Individual has an Eastern Cooperative Oncology Group performance status of 0-2 and no history of bleeding or thrombosis (Zalcman 2016, Ceresoli 2013);

OR

- B. Bevacizumab is used as maintenance therapy for unresectable disease, as a single agent, when:
 - 1. Bevacizumab was previously administered as an agent in a first-line combination regimen; **AND**
 - 2. Bevacizumab used until disease progression*;

*Note: Once disease progression has occurred, bevacizumab is not to be re-instituted.

OR

X. Individual has a diagnosis of non-squamous Non-Small Cell Lung Cancer (NSCLC) and the following are met:

- A. Individual has a current Eastern Cooperative Oncology Group performance status of 0-1, no history of hemoptysis; **AND**
- B. Individual is using for one of the following:
 - 1. As first-line therapy; **OR**

This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply.

Market Applicability							
Market	DC	GA	KY	MD	NJ	NY	WA
Applicable	X	X	X	X	X	X	X

2. As second-line therapy if tyrosine-kinase inhibitor (TKI/anaplastic lymphoma kinase (ALK) targeted agent was given as first-line therapy (NCCN 2A);

AND

- C. Individual is using for one of the following:
 1. Advanced, recurrent or metastatic disease in combination with platinum-based therapy and either a taxane or pemetrexed; **OR**
 2. Advanced, recurrent or metastatic disease in combination platinum-based therapy, a taxane and atezolizumab;

OR

- XI. Individual has a diagnosis of non-squamous Non-Small Cell Lung Cancer (NSCLC) and the following are met:
 - A. Individual is using as maintenance therapy when bevacizumab was previously administered as an agent in a first-line combination chemotherapy regimen and is used until disease progression, when:
 1. Individual has advanced, recurrent, or metastatic disease and using as a single agent; **OR**
 2. Individual has advanced, recurrent, or metastatic disease and using as a single agent or in combination with atezolizumab;

OR

- XII. Individual has a diagnosis of Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer and the following are met:
 - A. Bevacizumab is used for advanced or metastatic following initial surgical resection (as adjuvant therapy) when:
 1. Used in combination with other chemotherapy; **AND**
 2. Used in a single line of therapy;

OR

- B. Bevacizumab is used for recurrent, metastatic disease that is relapsed or refractory when:
 1. Used as a single agent or in combination with other Chemotherapy (NCCN 2A), Label); **AND**
 2. Used in a single line of therapy;

OR

- XIII. Individual has a diagnosis of Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer and the following criteria are met:
 - A. Bevacizumab is used as maintenance therapy for advanced, recurrent, or metastatic disease; **AND**
 - B. Was previously administered as an agent in a combination

Market Applicability							
Market	DC	GA	KY	MD	NJ	NY	WA
Applicable	X	X	X	X	X	X	X

- chemotherapy regimen (given first-line or following initial surgical resection); **AND**
- C. Used as a single agent; **AND**
- D. May be used until disease progression;

OR

- XIV. Individual has a diagnosis of Renal Cell Carcinoma (RCC) and the following are met:
- A. Individual has metastatic clear cell RCC and bevacizumab is used as first-line treatment in combination with interferon alpha; **OR**
 - B. Individual has relapsed or medically unresectable stage IV disease when:
 1. Bevacizumab is used as a single agent in those with predominant clear cell histology who have progressed on prior cytokine therapy (NCCN 2B; Yang 2003); **OR**
 2. Bevacizumab is used as a single agent in those with non-clear cell histology (NCCN 2A); **OR**
 3. Bevacizumab is used in combination with erlotinib or everolimus in those with non-clear cell histology (including papillary RCC and hereditary leiomyomatosis and RCC [HLRCC]) (NCCN 2A);

OR

- XV. Individual has a diagnosis of Soft Tissue Sarcoma and the following are met (NCCN 2A):
- A. Bevacizumab is used as a single agent for the treatment of angiosarcoma; **OR**
 - B. Bevacizumab is used in combination with temozolomide for the treatment of solitary fibrous tumor and hemangiopericytoma.

Requests for Avastin (bevacizumab), Mvasi (bevacizumab-awwb) may **not** be approved for the following:

- I. All other indications not included above; **OR**
- II. Individual is using as adjuvant therapy following surgery for stage II or III adenocarcinoma of the colon; **OR**
- III. Individual is using bevacizumab in combination with the same irinotecan based regimen that was previously used in combination with ziv-aflibercept; **OR**
- IV. Individual is using for treatment of a single condition with concomitant use of other targeted biologic agents (including cetuximab, panitumumab, trastuzumab, lapatinib and ziv-aflibercept); **OR**
- V. Individual is using for the treatment of any of the following:
 - A. Prostate cancer; **OR**
 - B. Carcinoid tumors; **OR**
 - C. Metastatic melanoma; **OR**
 - D. Metastatic adenocarcinoma of the pancreas; **OR**

This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply.

Market Applicability							
Market	DC	GA	KY	MD	NJ	NY	WA
Applicable	X	X	X	X	X	X	X

- E. Metastatic breast cancer, second line therapy or greater, for example when progression noted following anthracycline and taxane chemotherapy; **OR**
- F. Neurofibromatosis type 2; **OR**
- G. AIDS-related Kaposi sarcoma.

Note: Bevacizumab (Avastin, Mvasi) have black box warnings for gastrointestinal perforations, surgery and wound healing complications, and hemorrhage.

Gastrointestinal Perforations: The incidence of gastrointestinal perforation, some fatal, in patients receiving bevacizumab ranges from 0.3 to 3.2%. Discontinue bevacizumab in patients who develop gastrointestinal perforation.

Surgery and Wound Healing Complications: The incidence of wound healing and surgical complications, including serious and fatal complications, is increased in patients receiving bevacizumab. 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 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, hematemesis, central nervous system (CNS) hemorrhage, epistaxis, and vaginal bleeding occurred up to 5-fold more frequently in patients receiving bevacizumab. Do not administer bevacizumab to patients with a recent history of hemoptysis. Discontinue in patients who develop Grade 3-4 hemorrhage.

State Specific Mandates		
State name	Date effective	Mandate details (including specific bill if applicable)
N/A	N/A	N/A

Key References:

1. Allegra CJ, Yothers G, O'Connell MJ, Sharif S, Petrelli NJ, Lopa SH, Wolmark N. Bevacizumab in stage II-III colon cancer: 5-year update of the National Surgical Adjuvant Breast and Bowel Project C-08 trial. J Clin Oncol. 2013 Jan 20;31(3):359-64
2. Barlesi F, Scherpereel A, Gorbunova V, et al. Maintenance bevacizumab-pemetrexed after first-line cisplatin-pemetrexed-bevacizumab for advanced nonsquamous non-small-cell lung cancer: updated survival analysis of the AVAPERL (MO22089) randomized phase III trial. Ann Oncol. 2014; 25(5):1044-1052.
3. Barlesi F, Scherpereel A, Rittmeyer A, et al. Randomized phase III trial of maintenance bevacizumab with or without pemetrexed after first-line induction with bevacizumab, cisplatin, and pemetrexed in advanced nonsquamous non-small-cell lung cancer: AVAPERL (MO22089). J Clin Oncol. 2013; 31(24):3004-3011.
4. Ceresoli GL, Zucali PA, Mencoboni M, et al. Phase II study of pemetrexed and carboplatin plus bevacizumab as first-line therapy in malignant pleural mesothelioma. Br J Cancer. 2013; 109(3):552-558.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2018. URL: <http://www.clinicalpharmacology.com>. Updated periodically.

This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply.

Market Applicability							
Market	DC	GA	KY	MD	NJ	NY	WA
Applicable	X	X	X	X	X	X	X

6. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. <http://dailymed.nlm.nih.gov/dailymed/about.cfm>. Accessed: June 14, 2018.
7. de Gramont A, Van Cutsem E, Schmoll HJ, Tabernero J, Clarke S, Moore MJ, Cunningham D, Cartwright TH, Hecht JR, Rivera F, Im SA, Bodoky G, Salazar R, Maindrault-Goebel F, Shacham-Shmueli E, Bajetta E, Makrutzki M, Shang A, André T, Hoff PM. Bevacizumab plus oxaliplatin-based chemotherapy as adjuvant treatment for colon cancer (AVANT): a phase 3 randomised controlled trial. *Lancet Oncol*. 2012 Dec;13(12):1225-33
8. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
9. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2018; Updated periodically.
10. Uldrick TS, Wyvill KM, Kumar P, et al. Phase II study of bevacizumab in patients with HIV-associated Kaposi's sarcoma receiving antiretroviral therapy. *J Clin Oncol* 2012;30:1476-1483.
11. NCCN Clinical Practice Guidelines in Oncology™. © 2019 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: <http://www.nccn.org/index.asp>. Accessed April, 2019.
 - a. Central Nervous System Cancers. V1.2019. Revised March 5, 2019.
 - b. AIDS-Related Kaposi Sarcoma. V2.2019. Revised November 29, 2018.
 - c. Breast Cancer. V1.2019. Revised March 14, 2019.
 - d. Vulvar Cancer. V2.2019. Revised December 17, 2018.
 - e. Cervical Cancer. V4.2019. Revised March 29, 2019.
 - f. Colon Cancer. V1.2019. Revised March 15, 2019.
 - g. Malignant Pleural Mesothelioma. V2. 2019. April 1, 2019.
 - h. Uterine Neoplasms. 3.2019. February 11, 2019.
 - i. Ovarian Cancer. 1.2019. March 8, 2019.
 - j. Kidney Cancer. 3.2019. February 6, 2019.
 - k. Soft tissue sarcoma. 2.2019. February 4, 2019.
 - l. Non-Small Cell Lung Cancer. V3.2019. January 18,2019
12. Rittmeyer A, Gorbunova V, Vikström A, et al. Health-related quality of life in patients with advanced nonsquamous non-small-cell lung cancer receiving bevacizumab or bevacizumab-plus-pemetrexed maintenance therapy in AVAPERL (MO22089). *J Thorac Oncol*. 2013; 8(11):1409-1416.
13. Rose PG, Ali S, Moslemi-Kebria M, Simpkins F. Paclitaxel, carboplatin, and bevacizumab in advanced and recurrent endometrial carcinoma. *Int J Gynecol Cancer*. 2017; 27(3):452-458.
14. Simkens LH, van Tinteren H, May A, et al. Maintenance treatment with capecitabine and bevacizumab in metastatic colorectal cancer (CAIRO3): a phase 3 randomised controlled trial of the Dutch Colorectal Cancer Group. *Lancet*. 2015; 385(9980):1843-1852.
15. Tewari KS, Sill M, Long HJ, et al. Improved survival with bevacizumab in advanced cervical cancer. *N Engl J Med*. 2014; 370 (8):734-743.
16. Yang, JC, Haworth L, Sherry RM, et al. A randomized trial of bevacizumab, an anti-vascular endothelial growth factor antibody, for metastatic renal cancer. *N Engl J Med* 2003; 349:427-434.
17. Zalcman G, Mazieres J, Margery J, et al. Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS): a randomised, controlled, open-label, phase 3 trial. *Lancet*. 2016; 387(10026):1405-1414.

This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply.