Clinical Policy: Bevacizumab-awwb (Mvasi)

Reference Number: CP.PHAR.356
Effective Date: 10.17.17
Last Review Date: 11.17
Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Bevacizumab-awwb (Mvasi®) is a humanized monoclonal antibody against vascular endothelial growth factor (VEGF, also known as vascular permeability factor [VPF] or VEGF-A).

FDA Approved Indication(s)

Mvasi is indicated for the treatment of:

- Metastatic colorectal cancer, with intravenous 5-fluorouracil (5-FU)-based 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 bevacizumab product-containing regimen.
- Non-squamous, non-small cell lung cancer (NSCLC), 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 bevacizumab products.
- Metastatic renal cell carcinoma (RCC) with interferon alpha.
- Cervical cancer, in combination with paclitaxel and cisplatin or paclitaxel and topotecan in persistent, recurrent, or metastatic disease.

Limitation(s) of use: Mvasi is not indicated for adjuvant treatment of colon cancer.

Policy/Criteria

Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Centene Corporation® that Mvasi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Colorectal Cancer (must meet all):

1. Meets a or b:
    a. FDA-approved use:
        i. Colorectal cancer (a or b):
            1. Primary or subsequent therapy for metastatic disease:

a. In combination with 5-FU-based therapy;
2. Subsequent therapy for metastatic disease:
a. In combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based therapy after disease progression on a first-line bevacizumab product-containing regimen;

b. Off-label NCCN approved use:
i. Colorectal cancer (a or b):
a) Primary or subsequent therapy for unresectable, metastatic or medically inoperable disease (1, 2 or 3):
1) In combination with capecitabine, FOLFOX, FOLFIRI, CapeOX, FOLFOXIRI, or 5-FU/LV;
2) In combination with irinotecan;
3) In combination with irinotecan and oxaliplatin;
b) Adjuvant therapy for resectable metastases:
1) In combination with capecitabine, FOLFOX, FOLFIRI, CapeOX, FOLFOXIRI, or 5-FU/LV;
ii. Rectal cancer:
a) Primary therapy for resectable disease classified as either (T3/N0/M0 [stage IIA]) or (anyT/N1-2/M0 [stage III]):
1) In combination with capecitabine, FOLFOX, FOLFIRI, FOLFOXIRI, CapeOX, or 5-FU/LV;

2. Dose does not exceed one of the following (a or b):
a. Maximum dose indicated in Section V;
b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Non-Squamous Non-Small Cell Lung Cancer (must meet all):
1. Diagnosis of non-squamous NSCLC;
2. Meets a or b:
a. FDA-approved use:
i. Primary therapy for unresectable, locally advanced, recurrent or metastatic disease:
a) In combination with carboplatin and paclitaxel;
b. Off-label NCCN recommended use (i or ii):
i. Primary or subsequent therapy for unresectable, locally advanced, recurrent or metastatic disease (a, b, c or d):
1. In combination with carboplatin and paclitaxel;
2. In combination with carboplatin and pemetrexed;
3. In combination with pemetrexed;
4. In combination with cisplatin and pemetrexed;
ii. Continuation maintenance therapy (if prior bevacizumab-product use associated with achievement of tumor response or stable disease) (a or b):
a) As single agent;
b) In combination with pemetrexed;

3. Dose does not exceed one of the following (a or b):
   a. Maximum dose indicated in Section V;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

C. Glioblastoma (must meet all):
1. Diagnosis of glioblastoma;
2. Meets a or b:
   a. FDA-approved use:
      i. Subsequent therapy for recurrent or progressive disease;
         a) As single agent;
   b. Off-label NCCN recommended use:
      i. Subsequent therapy for recurrent disease:
         a) In combination with irinotecan, carmustine, lomustine, temozolomide, or carboplatin;
3. Dose does not exceed one of the following (a or b):
   a. Maximum dose indicated in Section V;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

D. Renal Cell Carcinoma (must meet all):
1. Diagnosis of RCC;
2. Meets a or b:
   a. FDA-approved use:
      i. Metastatic disease:
         1. In combination with interferon alfa-2a/2b;
   b. Off-label NCCN recommended use:
      i. Relapsed or stage IV (advanced or metastatic) disease (a or b):
         a) Clear cell histology - primary therapy:
            1) In combination with interferon alfa-2b;
         b) Non-clear cell histology:
            1) As single agent;
4. Dose does not exceed one of the following (a or b):
   a. Maximum dose indicated in Section V;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

E. Carcinoma of the Cervix (must meet all):
1. Diagnosis of cervical carcinoma;
2. Meets a or b:
   a. FDA-approved use:
      i. Persistent, recurrent or metastatic disease (a or b):

a) In combination with paclitaxel and cisplatin;
b) In combination with paclitaxel and topotecan;

b. Off-label NCCN recommended use:
i. Persistent, recurrent or metastatic disease as primary therapy (a or b):
a) In combination with carboplatin;
b) In combination with topotecan;

3. Dose does not exceed one of the following (a or b):
a. Maximum dose indicated in Section V;
b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

F. Other Compendia Supported Indications (off-label):

1. Oncology: The following off-label NCCN recommended uses meeting NCCN categories 1 and 2a are approvable:
a. Breast cancer: In combination with paclitaxel for recurrent or metastatic HER2-negative disease;
b. Ovarian cancer
c. Endometrial carcinoma that has progressed on prior cytotoxic chemotherapy;
d. Malignant pleural mesothelioma;
e. Primary central nervous system cancers (i or ii):
i. Adult intracranial and spinal ependymoma (excluding subependymoma);
ii. Anaplastic glioma;
f. Kidney Cancer
g. Rectal Cancer
h. Soft tissue sarcoma (i or ii):
i. Angiosarcoma;
ii. Solitary fibrous tumor/hemangiopericytoma in combination with temozolomide;
2. Ophthalmology (intravitreal administration):
a. Retinopathy of prematurity;
b. Neovascular glaucoma after failure of one approved antiglaucoma medication at maximally tolerated doses, unless contraindicated or clinically significant adverse effects are experienced;
c. Neovascular (wet) age-related macular degeneration confirmed by an ophthalmologist;
d. Proliferative diabetic retinopathy and patient will be undergoing vitrectomy;
e. Macular edema secondary to (i or ii):
i. Branch or central retinal vein occlusion;
ii. Diabetes;
f. Choroidal/retinal neovascularization secondary to (i or ii):
i. Pathologic myopia;
ii. Angioid streaks;
3. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

G. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PHAR.57 – Global Biopharm Policy.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Documentation supports that member is currently receiving Mvasi for one of the oncology diagnoses in Section I;
2. Member is responding positively to therapy (e.g., no disease progression, no significant toxicity, etc.)
3. Dose does not exceed one of the following (a or b):
   c. Maximum dose indicated in Section V;
   d. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Centene Corporation and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PHAR.57 or evidence of coverage documents.
B. Use as a single agent for metastatic carcinoma of the colon or rectum (bevacizumab as a single agent resulted in inferior survival rates when compared to FOLFOX regimen);
C. NSCLC with squamous histology (due to increased risk of hemoptysis);
D. Bevacizumab in combination with gemcitabine as first-line therapy for carcinoma of the pancreas (combination did not improve survival compared to gemcitabine monotherapy);
E. Bevacizumab monotherapy in hormone refractory prostate cancer;
F. Recent surgery (within the last 28 days) or surgical wounds that have not completely healed;
G. Members with gastrointestinal perforations, serious hemorrhage, or recent hemoptysis.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CapeOX: capecitabine/oxaliplatin
FDA: Food and Drug Administration
FOLFIRI: folinic acid/fluorouracil/irinotecan
FOLFOX: folinic acid/fluorouracil/oxaliplatin
FOLFOXIRI: fluorouracil/leucovorin/ oxaliplatin/irinotecan
NCCN: National Comprehensive Cancer Network
NSCLC: non-small cell lung carcinoma
5-FU: fluorouracil
5-FU/LV: fluorouracil/leucovorin

Appendix B: General Information

- The FDA revoked the approval of the breast cancer indication for bevacizumab on November 18, 2011. Bevacizumab 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 bevacizumab will either help women with breast cancer live longer or improve their quality of life.
- Fatal pulmonary hemorrhage can occur in patients with NSCLC treated with chemotherapy and bevacizumab. 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 bevacizumab.
- Bevacizumab has been added to the 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).
- Bevacizumab, 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.
- Bevacizumab 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 bevacizumab in neovascular glaucoma, one study did indicate the use of timolol, dorzolamide, and brimonidine before a bevacizumab injection.
- Bevacizumab 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.
- Bevacizumab is a category 2A, in the NCCN practice guidelines, for the treatment of adult intracranial and spinal ependymoma (excluding subependymoma).
- Bevacizumab is category 2A, in the NCCN practice guidelines, for the treatment of non-

clear cell renal carcinoma.

- Bevacizumab is category 2A, in the NCCN practice guidelines, for the treatment of endometrial carcinoma
- Bevacizumab in combination with cisplatin/paclitaxel has been added to the NCCN practice guidelines as category 1 for recurrent or metastatic cervical cancer.
- Bevacizumab 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).
- Bevacizumab has a black box warning for gastrointestinal perforation, surgery and wound healing complications, and hemorrhage. Bevacizumab should be discontinued in patients with wound dehiscence. Discontinue at least 28 days prior to elective surgery. Do not initiate bevacizumab for at least 28 days after surgery and until the surgery wound is fully healed. Bevacizumab 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. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
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 bevacizumab-containing regimen	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks.
Non-Squamous NSCLC	15 mg/kg IV infusion every 3 weeks with carboplatin/paclitaxel	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks.
Clear cell RCC	10 mg/kg IV every 2 weeks with interferon alfa	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks.
Glioblastoma Multiforme, Anaplastic Astrocytoma, Anaplastic Oligodendroglioma	10 mg/kg IV every 2 weeks	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks.
Soft tissue sarcoma	15 mg/kg IV infusion every 3 weeks	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 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	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks.
Neovascular (Wet) Macular Degeneration	1.25 to 2.5 mg administered by intravitreal injection every 4 weeks	2.5 mg/dose
Neovascular Glaucoma	1.25 mg administered by intravitreal injection every 4 weeks	2.5 mg/dose
Macular edema secondary to retinal vein occlusion	1 mg to 2.5 mg administered by intravitreal injection every 4 weeks	2.5 mg/dose
Proliferative diabetic retinopathy	1.25 mg administer by intravitreal injection 5 to 20 days before vitrectomy	2.5 mg/dose
Diabetic Macular Edema	1.25 mg administered by intravitreal injection	2.5 mg/dose
Malignant Mesothelioma of Pleura	15 mg/kg IV (plus pemetrexed 500 mg/m(2) IV and cisplatin 75 mg/m(2) IV) every 21 days for up to 6 cycles, followed by maintenance bevacizumab 15 mg/kg every 21 days until disease progression or unacceptable toxicity. All patients should receive folic acid 400 mcg orally daily and vitamin B12 1000 mcg IM every 3 weeks, both beginning 7 days prior to pemetrexed and continuing for 3 weeks following the last pemetrexed dose (off-label dosage).	2.5 mg/dose
Metastatic Colorectal Cancer in Previously Untreated Elderly Patients Ineligible for Oxaliplatin- or Irinotecan-based Chemotherapy	7.5 mg/kg IV on day 1 with capecitabine 1000 mg/m (2) orally twice daily on days 1 to 14, given every 3 weeks until disease progression.	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks.

VI. Product Availability

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

VII. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created. Policy based on existing Bevacizumab PA criteria (CP.PHAR.93 bevacizumab (Avastin))	10.17. 17	11.17

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.