Bevacizumab Agents (Avastin, Alymsys, Avzivi, Jobevne, Mvasi, Vegzelma, Zirabev)

Override(s)	Approval Duration
Prior Authorization	1 year

Medications	Dosing Limit (when used for ophthalmologic indications)
Avastin (bevacizumab) 100 mg, 400 mg vial Alymsys (bevacizumab-maly) 100 mg, 400 mg vial Avzivi (bevacizumab-tnjn) 100 mg, 400 mg vial Jobevne (bevacizumab-nwgd) 100 mg, 400 mg vial Mvasi (bevacizumab-awwb) 100 mg, 400 mg vial Vegzelma (bevacizumab-adcd) 100 mg, 400 mg vial Zirabev (bevacizumab-bvzr) 100 mg, 400 mg vial	1.25 mg per eye; each eye may be treated as frequently as every 4 weeks

APPROVAL CRITERIA

Prior Authorization for Ophthalmologic Indications

Requests for Avastin (bevacizumab), Alymsys (bevacizumab-maly), Mvasi (bevacizumab-awwb), Vegzelma (bevacizumab-adcd), or Zirabev (bevacizumab-bvzr) may be approved if the following criteria are met:

I. Individual has a diagnosis of one of the following:
   A. Diabetic macular edema (DME) (including DME with diabetic retinopathy of any severity) (AAO 2019); **OR**
   B. Proliferative or moderate to severe non-proliferative diabetic retinopathy with or without diabetic macular edema (AAO 2019 DP B IIa); **OR**
   C. Established neovascular “wet” age-related macular degeneration (AHFS); **OR**
   D. Macular edema from branch retinal vein occlusion (AAO 2019); **OR**
   E. Macular edema from central retinal vein occlusion (AAO 2019); **OR**
   F. Neovascular glaucoma (Costagliola 2008, DP B IIb); **OR**

G. Choroidal neovascularization associated with myoptic 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);

Requests for intravitreal injections of Avastin (bevacizumab), Alymsys (bevacizumab-maly), Mvasi (bevacizumab-awwb), Vegzelma (bevacizumab-adcd), Zirabev (bevacizumab-bvzr) may not be approved when the above criteria are not met and for all other indications.

Prior Authorization for Non-Ophthalmologic Indications

Requests for Avastin (bevacizumab), Alymsys (bevacizumab-maly), Avzivi (bevacizumab-tnjn), Jobevne (bevacizumab-nwgd), Mvasi (bevacizumab-awwb), Vegzelma (bevacizumab-adcd), or Zirabev (bevacizumab-bvzr) may be approved if the following criteria are met:

I. Individual has a diagnosis of Ampullary adenocarcinoma and the following are met (NCCN 2A):
    A. Bevacizumab is used in combination with a 5-fluorouracil-based (including capecitabine) regimen; **AND**
    B. Individual is using for a metastatic intestinal disease;

OR

II. Individual has a diagnosis of Central Nervous System – Primary Tumor and the following are met (Label, NCCN 2A):
    A. Individual has failed radiation therapy; **AND**
    B. Bevacizumab is used in a single line of therapy or as a single agent; **AND**
    C. The tumor to be treated includes but is not limited to:
        1. Adult medulloblastoma in combination with temozolomide and irinotecan; **OR**
        2. Adult intracranial and spinal ependymoma (excluding subependymoma) as a single agent only; **OR**
        3. IDH-mutant astrocytoma; **OR**
        4. Anaplastic glioma; **OR**
        5. Glioblastoma; **OR**
        6. Glioblastoma multiforme; **OR**
        7. High-grade glioma, recurrent or progressive; **OR**
        8. Meningiomas as a single agent only; **OR**

9. Oligodendroglioma IDH-mutant, 1Q19 codeleted;

OR

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

OR

IV. Individual is using bevacizumab as a single agent treatment for neurofibromatosis type 2 vestibular schwannomas with hearing loss (NCCN 2A);

OR

V. Individual has a diagnosis of pediatric central nervous system cancers and the following are met:

A. Bevacizumab is part of a treatment for recurrent or progressive disease when:

1. Used in combination for treatment of palliation in diffuse high-grade gliomas; **OR**
2. Used as part of TEMR (temzolomide, irinotecan, bevacizumab) regimen; **OR**
3. Used as part of MEMMAT (thalidomide, celecoxib, fenofibrate, etoposide, cyclophosphamide, bevacizumab regimen);

OR

VI. Individual has a diagnosis of advanced or metastatic colorectal, appendiceal, or anal adenocarcinoma and the following are met (Label, NCCN 2A):

A. Individual has not progressed on more than two lines of a bevacizumab-containing chemotherapy regimen (Simkens 2015); **AND**
B. Individual has either pMMR/MSS, dMMR/MSI-H, or POLE/POLD1 mutation with ultra-hypermutated phenotype [e.g. TMB >50 mut/Mb]; **AND**
C. Individual is ineligible or has progressed on checkpoint inhibitor immunotherapy; **AND**

1. Bevacizumab is used in combination with 5-fluorouracil-based (including capecitabine) chemotherapy, irinotecan, or oxaliplatin;

OR

2. Bevacizumab is used in combination with trifluridine and tipiracil (Lonsurf) in patients who have progressed through standard therapies;

OR

VII. Individual has a diagnosis of advanced or metastatic small bowel adenocarcinoma and the following are met (NCCN 2A):

A. Bevacizumab is used in combination with 5-fluorouracil-based (including capecitabine) regimen; **AND**
B. Bevacizumab is used as initial therapy or subsequent therapy for disease progression; **AND**
C. Bevacizumab is used in a single line of therapy; **AND**
D. Individual is pMMR/MSS (proficient mismatch repair/microsatellite-stable);

OR

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

A. Individual has advanced, recurrent or metastatic disease; **AND**
B. Used in one of the following ways:

1. Bevacizumab is used in combination with paclitaxel and either cisplatin or carboplatin; **AND**
2. Bevacizumab may be continued as maintenance therapy

OR

3. Bevacizumab is used in combination with pembrolizumab, paclitaxel, a platinum agent for PD-L1 positive disease; **AND**
4. Bevacizumab and pembrolizumab may be continued as maintenance therapy;

OR

IX. Individual has a diagnosis of Cervical Cancer, including vaginal cancer and the following are met (Label, NCCN 1, 2A):
- A. Individual has persistent, recurrent, or metastatic disease; **AND**
- B. Bevacizumab is used in a single line of therapy; **AND**
- C. Bevacizumab is being used in combination with paclitaxel and either topotecan, cisplatin, or carboplatin for disease that is not amenable to curative treatment with surgery or radiotherapy (Tewari 2014);
  OR
- D. Bevacizumab is used in combination with pembrolizumab, paclitaxel, and a platinum agent for PD-L1 positive disease; **OR**
- E. Bevacizumab is used as a single agent for second-line or subsequent therapy;

OR

X. Individual has a diagnosis of locally advanced, recurrent, or metastatic cervical cancer (NCCN 1); **AND**
- A. Individual is using bevacizumab in combination with atezolizumab, platinum-containing agent, and paclitaxel; **OR**
- B. Individual is using Bevacizumab in combination with atezolizumab for maintenance therapy;

OR

XI. Individual has a diagnosis of locally advanced, recurrent, or metastatic small cell neuroendocrine carcinoma of the cervix (NECC) (NCCN 2A); **AND**
- A. Individual is using in combination with paclitaxel and topotecan; **OR**
- B. As second-line or subsequent therapy as a single agent;

OR

XII. Individual has a diagnosis of Endometrial Carcinoma and the following are met (NCCN 2A):
- A. Individual has advanced or recurrent disease; **AND**
- B. Bevacizumab is being used in combination with carboplatin and paclitaxel;
  OR
- C. Following combination therapy with carboplatin and paclitaxel, bevacizumab is being used as single-agent maintenance therapy until disease progression or prohibitive toxicity;

OR

XIII. Individual has a diagnosis of Malignant Pleural or Peritoneal Mesothelioma (including pericardial mesothelioma and tunica vaginalis testis) and the following are met (NCCN 1, 2A):

A. Bevacizumab is used as first-line therapy for Malignant Pleural Mesothelioma unresectable disease or Peritoneal Mesothelioma when (DP A IIa):
   1. Used in 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); **AND**
   3. Individual is not eligible for surgery;

OR

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

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

OR

C. Bevacizumab is used as subsequent systemic therapy for Malignant Pleural or Peritoneal Mesothelioma, if immunotherapy was administered as first-line treatment in combination with pemetrexed and cisplatin or carboplatin (in those not eligible for cisplatin); **OR**

D. Bevacizumab is used as subsequent systemic therapy for Malignant Peritoneal Mesothelioma in combination with atezolizumab if individual has not previously been treated with immune checkpoint inhibitors;

OR

IX. Individual has a diagnosis of recurrent, advanced, or metastatic non-squamous Non-Small Cell Lung Cancer (NSCLC) and the following are met (NCCN 2A):

A. Individual has a current ECOG performance status of 0-2, no history of hemoptysis; **AND**
B. Individual has EGFR positive mutations; **AND**
C. Individual is using in combination with erlotinib; **AND**
D. Individual is using for one of the following:
   1. As first-line therapy; **OR**
   2. As continuation of therapy following disease progression of erlotinib with bevacizumab for asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited progression (if T790M negative);

OR

X. Individual has a diagnosis of advanced, recurrent, or metastatic non-squamous Non-Small Cell Lung Cancer (NSCLC) and the following are met (Label, NCCN 1, 2A):
   A. Individual has a current Eastern Cooperative Oncology Group performance status of 0-2, no history of hemoptysis; **AND**
   B. Individual is using in combination with platinum-based therapy, and either a taxane, or pemetrexed ; **AND**
   C. Individual is using for one of the following:
      1. As first line therapy (Label); **OR**
      2. As subsequent therapy if disease has progressed during or following treatment with a targeted agent for the expressed oncogene (including but not limited to, kinase inhibitors that target EGFR, KRAS, ALK, ROS1, BRAF, NTRK, RET, NRG1, ERBB2 (HER2) or MET mutations) (NCCN 2A);

OR

XI. Individual has a diagnosis of advanced, recurrent, or metastatic non-squamous Non-Small Cell Lung Cancer (NSCLC) and the following are met (NCCN 1):
   A. Individual has a current Eastern Cooperative Oncology Group performance status of 0-2, no history of hemoptysis; **AND**
   B. Individual does not have any contraindications for treatment with PD-1/PD-L1 inhibitors which include but not limited to active or previously documented autoimmune disease and /or current use of immunosuppressive agents; **AND**
   C. Individual is using in combination with platinum-based therapy, a taxane, and atezolizumab; **AND**
   D. Individual is using for one of the following:
      1. As first line therapy for PD-L1 expression positive (≥ 1%) tumors and if individual does not have presence of actionable molecular markers* (may be KRAS G12C mutation positive); **OR**
      2. As subsequent therapy if disease has progressed during or following treatment with a targeted agent for the expressed oncogene (including but not limited to, kinase inhibitors that target EGFR, KRAS, ALK, ROS1, BRAF, NTRK, RET, NRG1, ERBB2 (HER2) or MET mutations) (NCCN 2A);

OR

XII. Individual has a diagnosis of non-squamous Non-Small Cell Lung Cancer (NSCLC) and the following are met (NCCN 1):
   A. Individual is using as maintenance therapy for advanced, recurrent, or metastatic disease; **AND**
   B. Bevacizumab was previously administered as an agent in a first-line combination chemotherapy regimen; **AND**
   C. Individual is using as a single agent (DP B IIa), in combination with pemetrexed, or in combination with atezolizumab; **AND**
   D. May be used until disease progression;

OR

XIII. Individual has a diagnosis of Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer for stages II-IV disease and the following are met:

A. Bevacizumab is used for advanced or metastatic disease following initial surgical resection (as adjuvant therapy) when (NCCN 1):

1. Used in combination with other chemotherapy (except oxaliplatin and docetaxel in Grade 1 endometrioid and low-grade serous borderline epithelial ovarian cancer); **AND**
2. Used as maintenance therapy as a single agent;

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 as maintenance therapy as a single agent;
   OR
3. Used in combination with mirvetuximab soravtansine-gynx for FRα-expressing tumor for recurrent or platinum-resistant persistent disease (NCCN 2A); **OR**
4. Used in combination with other chemotherapy for platinum-resistant persistent disease (except in combination with ixabepilone) (NCCN 2A);

OR

XIV. Individual has a diagnosis of Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer for stage II-IV disease and the following criteria are met:

A. Bevacizumab is used as maintenance therapy for advanced, recurrent, or metastatic disease (NCCN 2A); **AND**
B. Was previously administered as an agent in a combination chemotherapy regimen; **AND**
C. Used as a single agent; **AND**
D. May be used until disease progression; **OR**
E. Bevacizumab used in combination with olaparib or niraparib (if unable to tolerate olaparib) when the following applies (NCCN 1, 2A, Lynparza label):

1. Individual has achieved complete clinical remission (CR) or partial remission (PR) to primary therapy; **AND**
2. Individual has a homologous recombination deficiency (HRD) positive status defined by either:
   a. Deleterious germline and/or somatic BRCA 1/2 mutation with test results confirmed; **OR**
   b. Genomic instability;

OR

XV. Individual has a diagnosis of Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer and the following are met (NCCN 1, 2A):

A. Individual is using in combination with carboplatin and either paclitaxel or docetaxel OR with oxaliplatin and docetaxel and individual is a poor surgical candidate or has a low likelihood of optimal cytoreduction; **AND**

B. Individual is using in one of the following ways:
    1. Bevacizumab as neoadjuvant therapy (except oxaliplatin and docetaxel in Grade I endometroid carcinoma); **OR**
    2. Bevacizumab as adjuvant therapy if individual has stable disease following neoadjuvant therapy;

OR

XVI. Individual has a diagnosis of Hepatocellular Carcinoma and the following are met (Label, NCCN 1):
A. Individual has advanced, unresectable, or metastatic disease; **AND**
B. Using in one of the following ways in combination with atezolizumab:
    1. As first-line treatment **OR**
    2. As subsequent-line systemic therapy (NCCN 2A); **AND**
C. Individual has Child-Pugh Class A or B liver function (NCCN 1, 2A); **AND**
D. Individual has an ECOG performance status of 0-2; **AND**
E. Bevacizumab may be used until disease progression;

OR

XVII. Individual has a diagnosis of Renal Cell Carcinoma (RCC) and the following are met:
A. Individual has metastatic RCC and bevacizumab is used in combination with interferon alpha (Label); **OR**
B. Individual has relapsed or medically unresectable stage IV disease when:
    1. Bevacizumab is used as a single agent in those with non-clear cell histology (NCCN 2A); **OR**
    2. 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

XVIII. 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**

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I. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to one preferred agent [Avastin (bevacizumab) or Mvasi (bevacizumab-awwb)];

OR

II. Individual is currently stabilized on the requested non preferred agent [Avastin

(bevacizumab), Alymsys (bevacizumab-maly), Avzivi (bevacizumab-tnjn), Jobevne (bevacizumab-nwgd), Vegzelma (bevacizumab-adcd), or Zirabev (bevacizumab-bvzr)].

Requests for Avastin (bevacizumab), Alymsys (bevacizumab-maly), Avzivi (bevacizumab-tnjn), Jobevne (bevacizumab-nwgd), Mvasi (bevacizumab-awwb), Vegzelma (bevacizumab-adcd), or Zirabev (bevacizumab-bvzr) may not be approved for the following:

I. All other non-ophthalmologic 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**
   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; **OR**
   H. Pseudoprogression of glioblastoma.

*__Note__: Actionable molecular markers include but not limited to EGFR, KRAS, ALK, ROS1, BRAF, NTRK, ERBB2 (HER2), MET and RET mutations. The NCCN panel recommends testing prior to initiating therapy to help guide appropriate treatment. If there is insufficient tissue to allow testing for all of these markers, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes (NCCN 2A).

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    a. Ampullary Adenocarcinoma. V2.2025. Revised January 10, 2025.
    b. Central Nervous System Cancers. V5.2024. Revised March 18, 2025.
    c. Cervical Cancer. 4.2025. Revised March 24, 2025.
    d. Colon Cancer. V1.2025. Revised February 7, 2025.
    e. Hepatocellular Carcinoma. V1.2025. Revised March 20, 2025.
    f. Malignant Peritoneal Mesothelioma. V2. 2025. January 14, 2025.
    g. Malignant Pleural Mesothelioma. V2.2025. January 14, 2025.
    h. Ovarian Cancer. 1.2025. Revised March 5, 2025.
    i. Pediatric Central Nervous System Cancers. V2.2025. Revised January 17, 2025.
    j. Kidney Cancer. V3.2025. Revised January 9, 2025.
    k . Non-Small Cell Lung Cancer. V3.2025. Revised January 14, 2025.
    l. Small Bowel Adenocarcinoma. V3.2025. Revised March 31, 2025.
    m. Soft tissue sarcoma. V5.2024. Revised March 10, 2025.
    n. Rectal Cancer. V2. 2025. Revised March 31, 2025.
    o. Uterine Neoplasms. 3.2025. March 7, 2025.
    p. Vaginal Cancer. V1.2025. Revised March 26, 2024.
    q. Vulvar Cancer. V1.2025. Revised February 10, 2025.
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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.