Medical Policy:

Bevacizumab Intravenous: Avastin, Alymsys, Mvasi, Vegzelma, Zirabev

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.70	November 20, 2024	February 2019

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Bevacizumab is a recombinant humanized monoclonal IgG1 antibody that binds to vascular endothelial growth factor (VEGF) and inhibits the proliferation of endothelial cells and the formation of new blood vessels.

Length of Authorization

- Coverage will be provided for **6 months** and may be renewed.
- For Adult **CNS cancers** (Symptom management), coverage will be provided for 12 weeks and may **NOT** be renewed.

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

Oncology indications (J9035/Q5107/Q5118/Q5126/Q5129):

− CRC, CNS Cancers, RCC:

o 120 billable units per 14 days

− NSCLC, Cervical Cancer, HCC, PM:

o 170 billable units per 21 days

− All other indications:

o 170 billable units per 14 days

Guideline

I. INITIAL APPROVAL CRITERIA

****For Medicare members – bevacizumab -please refer to our separate LCD/NCD Medicare criteria**

For Commercial, Medicaid, and Medicare members:

- Non-preferred agent: Avastin, Alymsys, Vegzelma
- Preferred agents: Mvasi, Zirabev.

Coverage is provided for the following conditions *(in addition to use supported by the National Comprehensive Cancer Network [NCCN] Clinical Practice Guidelines [NCCN Guidelines®] and/or NCCN Drugs & Biologics Compendium [NCCN Compendium®] with a recommendation of category level 1 or 2A*)*:

1. Patient is 18 years of age or older, unless otherwise specified; **AND**
2. Must be prescribed by or in consultation with an oncologist; **AND**
3. Patient does not have recent history of hemorrhage or hemoptysis (the presence of blood in sputum); **AND**
4. Patient must not have had a surgical procedure within the preceding 28 days or have a surgical wound that has not fully healed; **AND**
5. For newly started Avastin, Alymsys, or Vegzelma therapy, for Commercial, Medicaid, and Medicare members:

Coverage may be considered medically necessary when:

- Patient has experienced a therapeutic failure or intolerance with the plan-preferred medications (Mvasi AND Zirabev); **OR**
- Avastin, Alymsys or Vegzelma is requested for an indication for which the plan-preferred biosimilar agents (Mvasi or Zirabev) have not been FDA-approved OR are not supported by NCCN Guidelines® or NCCN Compendium® with a recommendation of category level 1 or 2A; **AND**

**Please note: Coverage for an appropriate biosimilar substitution will be allowed where NCCN Guidelines or Compendium state that an FDA-approved biosimilar is an appropriate substitution for bevacizumab.*

Hepatocellular Carcinoma (HCC)

1. Used as first-line therapy in combination with atezolizumab; **AND**

A. Patient has unresectable or metastatic disease †; **OR**

B. Patient has liver-confined disease that is inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic disease; **AND**

i. Patient has Child-Pugh Class A or B hepatic impairment; **OR**

C. Patient has extensive liver tumor burden; **AND**

i. Patient has Child-Pugh Class A or B hepatic impairment

Colorectal Cancer (CRC) † ‡

1. Will not be used as part of adjuvant treatment; **AND**

   A. Used in combination with a fluoropyrimidine- (e.g., 5-fluorouracil/5-FU or capecitabine) based regimen as first-line or subsequent therapy for metastatic, unresectable (or medically inoperable), or advanced disease; **AND**

      i. Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**

      ii. Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**

         a. Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy; **OR**

   B. Used in combination with irinotecan as initial treatment for unresectable metastatic disease; **AND**

      i. Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **AND**

      ii. Patient received previous FOLFOX or CapeOX within the past 12 months; **OR**

   C. Used in combination irinotecan as subsequent therapy for advanced or metastatic disease; **AND**

      i. Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**

      ii. Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**

         a. Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy; **OR**

   D. Used in combination with a fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatinbased regimen (not used first line) as second-line therapy for metastatic disease that has progressed on a first-line bevacizumab-containing regimen †; **OR**

   E. Used in combination with trifluridine and tipiracil as subsequent therapy for advanced or metastatic disease; **AND**

      i. Patient progressed through all available regimens (e.g., oxaliplatin-based therapy, irinotecan-based therapy, fluoropyrimidine-based therapy, etc.)*; **AND**

         a. Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**

         b. Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**

            1.) Patient is not eligible for or has progressed on checkpoint inhibitor

            immunotherapy; **OR**

   F. Used as primary treatment for T3, N Any; T1-2, N1-2; T4, N Any rectal cancer; **AND**

      i. Used in combination with a fluoropyrimidine- (e.g., 5-fluorouracil/5-FU or capecitabine) based regimen; **AND**

         a. Used if resection is contraindicated following total neoadjuvant therapy; **AND**

            1.) Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**

2.) Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**

- Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy; **OR**

b. Used if resection is contraindicated following neoadjuvant/definitive immunotherapy; **AND**

1.) Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease

**Refer to NCCN Colon and Rectal Cancer guidelines for regimens.*

Non-squamous non-small cell lung cancer (NSCLC) † ‡

1. Used for recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease with no evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**

A. Used as first-line therapy; **AND**

i. Used in combination with erlotinib for EGFR exon 19 deletion or exon 21 L858R mutations; **OR**

ii. Used for **ONE** of the following:

a. Patients with a performance status (PS) 0-1 who have tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) and PD-L1 expression < 1%; **OR**

b. PD-L1 expression positive (PD-L1 ≥ 1%) tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive); **OR**

c. Patients with a PS 0-1 who are positive for one of the following molecular biomarkers: EGFR exon 20, BRAF V600E, NTRK1/2/3 gene fusion, MET exon 14 skipping, RET rearrangement, or ERBB2 (HER2); **AND**

1.) Used in combination with **ONE** of the following:

– Carboplatin and paclitaxel †

– Pemetrexed AND either carboplatin or cisplatin in patients with contraindications¥ to PD-1 or PD-L1 inhibitors

– Atezolizumab, carboplatin, and paclitaxel; **OR**

B. Used as subsequent therapy in patients with a PS 0-1; **AND**

i. Used for **ONE** of the following:

a. EGFR exon 19 deletion or exon 21 L858R mutation, EGFR S768I, L861Q, and/or G719X mutation, ALK rearrangement, or ROS1 rearrangement positive tumors AND patient received prior targeted therapy§ for those aberrations; **OR**

b. BRAF V600E mutation, NTRK1/2/3 gene fusion, MET exon 14 skipping mutation, or RET rearrangement positive tumors; **OR**

c. PD-L1 expression positive (PD-L1 ≥ 1%) tumors that are negative for actionable molecular biomarkers* after prior PD-1/PD-L1 inhibitor therapy but no prior platinum-containing chemotherapy; **AND**

ii. Used in combination with **ONE** of the following:

a. Carboplatin and paclitaxel in patients with contraindications¥ to PD-1 or PDL1 inhibitors; **OR**

b. Pemetrexed AND either carboplatin or cisplatin in patients with contraindications¥ to PD-1 or PD-L1 inhibitors; **OR**

c. Atezolizumab, carboplatin, and paclitaxel (excluding use in patients who have received prior PD-1/PD-L1 inhibitor therapy); **OR**

C. Used as continuation maintenance therapy in patients who achieved a tumor response or stable disease after first-line systemic therapy; **AND**

i. Used as a single agent (bevacizumab must have been included in the first-line regimen); **OR**

ii. Used in combination with pemetrexed following a first-line bevacizumab/pemetrexed/platinum

chemotherapy regimen; **OR**

iii. Used in combination with atezolizumab following a first-line atezolizumab/carboplatin/paclitaxel/bevacizumab regimen; **OR**

D. Used as continuation of therapy following disease progression on erlotinib with bevacizumab; **AND**

i. Patient has asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited progression; **AND**

ii. Patient has T790M negative disease

**Note: Actionable molecular genomic biomarkers include EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2). Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2), via biopsy and/or plasma testing. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes.*

¥ Note: Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R, ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

Cervical Cancer † ‡

1. Disease has adenocarcinoma, adenosquamous, or squamous cell carcinoma histology; **AND**

   A. Patient has recurrent or metastatic disease; **AND**

      i. Used in combination with paclitaxel AND either cisplatin, carboplatin, or topotecan; **OR**

      ii. Used in combination with pembrolizumab, paclitaxel, AND cisplatin or carboplatin; **AND**

         a. Tumor expresses PD-L1 (Combined Positive Score [CPS] ≥1) as determined by an FDA-approved or CLIA compliant test; **OR**

      iii. Used as a single agent as subsequent therapy; **OR**

2. Patient has small cell neuroendocrine carcinoma of the cervix (NECC); **AND**

   B. Patient has persistent, recurrent, or metastatic disease; **AND**

      i. Used in combination with paclitaxel and topotecan; **OR**

      ii. Used as a single agent as subsequent therapy

Renal cell carcinoma (RCC)

1. Used in combination with interferon alfa for metastatic disease †; **OR**

1. Patient has relapsed or metastatic disease with non-clear cell histology; **AND**

   A. Used as a single agent ‡; **OR**

   B. Used in combination with everolimus ‡; **OR**

   C. Used in combination with erlotinib for advanced papillary disease including hereditary leiomyomatosis and renal cell carcinoma (HLRCC)-associated RCC ‡

Adult Central nervous system (CNS) cancer

1. Used as single-agent short-course therapy for symptom management related to radiation necrosis, poorly controlled vasogenic edema, or mass effect; **AND**

A. Patient has a diagnosis of **ONE** of the following CNS cancers ‡:

i. Circumscribed Glioma

ii. Primary CNS Lymphoma

iii. Meningiomas

iv. Brain or Spine metastases

v. Medulloblastoma

vi. Glioblastoma/Gliosarcoma/H3-mutated high-grade glioma

vii. IDH-mutant Astrocytoma (WHO Grade 2-4)

viii. IDH-mutant, 1p19q codeleted Oligodendroglioma (WHO Grade 2 or 3)

ix. Intracranial or Spinal Ependymoma (excluding subependymoma); **OR**

2. Used for recurrent or progressive disease; **AND**

A. Patient has a diagnosis of **ONE** of the following CNS cancers:

i. IDH-mutant, 1p19q codeleted Oligodendroglioma (WHO Grade 3) ‡

ii. Glioblastoma/Gliosarcoma/H3-mutated high-grade glioma † ‡

iii. IDH-mutant Astrocytoma (WHO Grade 3 or 4) ‡; **AND**

a. Used as a single agent; **OR**

b. Used in combination with carmustine, lomustine, or temozolomide; **AND**

1.) Patient has failed bevacizumab monotherapy; **OR**

B. Used as a single agent for Intracranial or Spinal Ependymoma (excluding subependymoma) after prior radiation therapy ‡; **OR**

C. Used as a single agent for surgically inaccessible Meningiomas when radiation is not possible ‡

Ovarian Fallopian Tube, and Primary Peritoneal Cancer † ‡ Φ

1. Patient has malignant stage II-IV sex cord-stromal tumors ‡; **AND**

A. Used as a single agent for clinically relapsed disease; **OR**

2. Patient has epithelial* ovarian, fallopian tube, or primary peritoneal cancer †; **AND**

A. Patient has persistent or recurrent disease; **AND**

i. Bevacizumab has not been used previously; **AND**

ii. Patient is not experiencing an immediate biochemical relapse (i.e., rising CA-125 without radiographic evidence of disease); **AND**

a. Patient has platinum-sensitive disease; **AND**

1. Used as a single agent; **OR**

2. Used in combination with carboplatin AND either gemcitabine, paclitaxel† or liposomal doxorubicin; **OR**

b. Patient has platinum-resistant disease; **AND**

1. Used as a single agent; **OR**

2. Used in combination with one of the following: oral cyclophosphamide, gemcitabine, liposomal doxorubicin, paclitaxel, or topotecan; **OR**

3. Used in combination with oral cyclophosphamide and pembrolizumab; **OR**

4. Used in combination with mirvetuximab soravtansine-gynx (in folate receptor-alpha expressing tumors); **OR**

5. Used in combination with carboplatin **AND** either gemcitabine, paclitaxel or liposomal doxorubicin; **OR**

B. Used in combination with paclitaxel and carboplatin for rising CA-125 levels or clinical relapse in patients who have received no prior chemotherapy (mucinous, clear cell, carcinosarcoma, endometrioid, and high-grade serous histology only); **OR**

C. Used in combination with paclitaxel and carboplatin for recurrence in patients who have received no prior chemotherapy (low-grade serous histology only); **OR**

D. Used as maintenance therapy; **AND**

i. Used for stage II-IV disease following primary therapy including bevacizumab; **AND**

a. Used as a single agent in patients that are BRCA1/2 wild-type or unknown **AND** homologous recombination (HR) proficient, HR deficient, or status unknown(grade 2/3 endometrioid and high-grade serous histology only); **OR**

1.) Used in combination with olaparib or niraparib (if unable to tolerate olaparib); **AND**

– Patient is BRCA1/2 wild-type or unknown AND HR deficient (grade 2/3 endometrioid and high-grade serous histology only); **OR**

– Patient has a germline or somatic BRCA1/2 mutation (grade 2/3 endometrioid, high-grade serous, clear cell, carcinosarcoma histology only); **OR**

b. Used as a single agent following recurrence therapy with chemotherapy plus bevacizumab for platinum-sensitive disease; **OR**

c. Used as continued treatment for stable disease following neoadjuvant therapy (*endometrioid and serous histology only*); **AND**

1.) Used in combination with carboplatin AND paclitaxel or docetaxel; **OR**

2.) Used in combination with oxaliplatin and docetaxel; **OR**

E. Used as neoadjuvant therapy (endometrioid and serous histology only); **AND**

i. Used in combination with one of the following:

a. Carboplatin AND paclitaxel or docetaxel

b. Oxaliplatin and docetaxel; **AND**

ii. Patient is a poor surgical candidate or has a low likelihood of optimal cytoreduction; **OR**

F. Used as adjuvant therapy; **AND**

i. Used in combination with oxaliplatin and docetaxel; **AND**

a. Patient has pathologic stage II-IV disease (mucinous, clear cell, carcinosarcoma,grade 2/3 endometrioid, and high-grade serous histology only); **OR**

b. Used following interval debulking surgery (IDS) in patients with a response or stable disease to neoadjuvant therapy (endometrioid and serous histology only); **AND**

1.) Patient is a poor surgical candidate or has a low likelihood of optimal cytoreduction; **OR**

ii. Used in combination with carboplatin **AND** paclitaxel or docetaxel; **AND**

a. Patient has pathologic stage II-IV disease; **OR**

b. Used following interval debulking surgery (IDS) in patients with a response or stable disease to neoadjuvant therapy (endometrioid and serous histology only); **AND**

1.) Patient is a poor surgical candidate or has a low likelihood of optimal cytoreduction

**Epithelial subtypes include serous, endometrioid, carcinosarcoma (malignant mixed Müllerian tumors [MMMTs] of the ovary), clear cell, mucinous, and borderline epithelial tumors (also known as low malignant potential [LMP] tumors).*

Soft tissue Sarcoma ‡

1. Used as a single agent for Angiosarcoma; **OR**
2. Used in combination with temozolomide for Solitary Fibrous Tumor

Endometrial Carcinoma (Uterine Neoplasms) ‡

1. Patient has recurrent disease; **AND**

A. Used as a single agent; **AND**

i. Used as subsequent therapy for disease that has progressed on prior cytotoxic chemotherapy; **OR**

ii. Used as continuation maintenance therapy following use in combination with carboplatin and paclitaxel; **OR**

B. Used in combination with carboplatin and paclitaxel

Malignant Pleural Mesothelioma (PM)‡

1. Used as first-line therapy; **AND**

A. Used in combination with pemetrexed AND either cisplatin or carboplatin (if cisplatin ineligible)**; AND**

i. Patient has clinical stage I–IIIA disease with epithelioid histology; **OR**

ii. Patient has clinical stage IIIB or IV disease, sarcomatoid or biphasic histology, or medically inoperable disease; **OR**

2. Used as subsequent therapy; **AND**

1. Used in combination with pemetrexed **AND** either cisplatin or carboplatin (if cisplatin ineligible); **AND**

i. Immunotherapy was administered as first-line treatment; **OR**
ii. Used as a rechallenge if pemetrexed-based treatment was administered first-line with good response

**Note: May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

§ Genomic Aberration/Mutational Driver Targeted Therapies (Note: not all inclusive, refer to guidelines for appropriate use)			
EGFR exon 19 deletion or exon 21 L858R tumors	**EGFR S768I, L861Q, and/or G719X mutation positive tumors**	**EGFR exon 20 insertion mutation positive tumors**	**NTRK1/2/3 gene fusion positive tumors**
− Afatinib − Erlotinib − Dacomitinib − Gefitinib − Osimertinib − Amivantamab	− Afatinib − Erlotinib − Dacomitinib − Gefitinib − Osimertinib − Amivantamab	− Amivantamab	− Larotrectinib − Entrectinib
ALK rearrangement-positive tumors	**ROS1 rearrangement-positive tumors**	**BRAF V600E-mutation positive tumors**	**ERBB2 (HER2) mutation positive tumors**
− Alectinib − Brigatinib − Ceritinib − Crizotinib − Lorlatinib	− Ceritinib − Crizotinib − Entrectinib − Lorlatinib − Repotrectinib	− Dabrafenib ± trametinib − Encorafenib + binimetinib − Vemurafenib	− Fam-trastuzumab deruxtecan-nxki − Ado-trastuzumab emtansine
PD-L1 tumor expression ≥ 1%	**MET exon-14 skipping mutations**	**RET rearrangement-positive tumors**	**KRAS G12C mutation positive tumors**
− Pembrolizumab − Atezolizumab − Nivolumab + ipilimumab − Cemiplimab − Tremelimumab + durvalumab	− Capmatinib − Crizotinib − Tepotinib	− Selpercatinib − Cabozantinib − Pralsetinib	− Sotorasib − Adagrasib

II. RENEWAL CRITERIA

Coverage can be renewed based upon the following criteria:

1. If request is for Avastin, Alymsys, Vegzelma ONLY: Continuation of documented current and/or successful therapy with a non-preferred agent (Avastin, Alymsys, Vegzelma); **AND**
2. Tumor response with stabilization of disease or decrease in size of tumor or tumor spread; **AND**
1. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: gastrointestinal perforation, surgical/wound healing complications, hemorrhage, arterial and venous thromboembolic events (ATE & VTE), uncontrolled hypertension, posterior reversible encephalopathy syndrome (PRES), nephrotic syndrome, severe infusion reactions, ovarian failure, congestive heart failure (CHF), etc.; **AND**
2. **CNS Cancers – symptom management (short-course therapy):** May NOT be renewed

3. **Ovarian cancer - Platinum sensitive disease or recurrence:** Must be used as a single agent for maintenance therapy; **OR** Used in combination with chemotherapy, for completion of initial therapy, up to 10 cycles total

Dosing/Administration

Indication	Dose
CRC	5 to 10 mg/kg every 2 weeks or 7.5 mg/kg every 3 weeks
NSCLC & Cervical Cancer	15 mg/kg every 3 weeks until disease progression or unacceptable toxicity.
Adult CNS Cancers	• For disease treatment: 10 mg/kg every 2 weeks until disease progression or unacceptable toxicity. • For symptom management: 5-10 mg/kg every 2 weeks up to 12 weeks duration
RCC	10 mg/kg every 2 weeks until disease progression or unacceptable toxicity.
MPM	15 mg/kg every 3 weeks in combination with chemotherapy for up to 6 cycles followed by single agent use, at the same dose/frequency, until disease progression or unacceptable toxicity.
Ovarian Cancer	Platinum-sensitive: 15 mg/kg every 3 weeks for up to 8 cycles when used with paclitaxel or up to 10 cycles when used with gemcitabine; followed by single-agent bevacizumab 15 mg/kg IV every 3 weeks until disease progression or unacceptable toxicity Platinum-resistant: 10 mg/kg every 2 weeks or 15 mg/kg every 3 weeks until disease progression or unacceptable toxicity
All Other Oncology Indications	5-10 mg/kg every 2 weeks **OR** 7.5-15 mg/kg every 3 weeks

Applicable Procedure Codes

Code	Description
J9035	Injection, bevacizumab, 10 mg; 1 billable unit = 10 mg
Q5126	Injection, bevacizumab-maly, biosimilar, (alymsys), 10 mg
Q5129	Injection, bevacizumab-adcd (vegzelma), biosimilar, 10 mg
Q5107	Injection, bevacizumab-awwb, biosimiliar, (Mvasi) 10 mg
Q5118	Injection, bevacizumab-bvcr, biosimilar, (Zirabev), 10 mg, effective 10/01/2019

Applicable NDCs

Code	Description
50242-0060-xx	Avastin single-use vial, 100 mg/4 mL solution for injection
50242-0061-xx	Avastin single-use vial, 400 mg/16 mL solution for injection
70121-1754-xx	Alymsys single-dose vial, 100 mg/4 mL solution for injection
70121-1755-xx	Alymsys single-dose vial, 400 mg/16 mL solution for injection
32228-0011-xx	Vegzelma single-dose vial, 100 mg/4 mL solution for injection
32228-0012-xx	Vegzelma single-dose vial, 400 mg/16 mL solution for injection
55513-0206-01	Mvasi single-use vial, 100 mg/4ml solution for injection
55513-0207-01	Mvasi single-use vial, 400 mg/16 mL solution for injection

00069-0315-01	Zirabev (bevacizumab-bvzr) injection single dose vial 100 mg/4 mL (25 mg/mL)
00069-0342-01	Zirabev (bevacizumab-bvzr) injection single dose vial 400 mg/16 mL (25 mg/mL)

ICD-10 Diagnoses

Code	Description
C17.0	Malignant neoplasm duodenum
C17.1	Malignant neoplasm jejunum
C17.2	Malignant neoplasm ileum
C17.8	Malignant neoplasm of overlapping sites of small intestines
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of large intestines
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C38.4	Malignant neoplasm of pleura
C45.0	Mesothelioma of pleura
C46.0	Kaposi's sarcoma of skin
C46.1	Kaposi's sarcoma of soft tissue
C46.2	Kaposi's sarcoma of palate

C46.3	Kaposi's sarcoma of lymph nodes
C46.4	Kaposi's sarcoma of gastrointestinal sites
C46.50	Kaposi's sarcoma of unspecified lung
C46.51	Kaposi's sarcoma of right lung
C46.52	Kaposi's sarcoma of left lung
C46.7	Kaposi's sarcoma of other sites
C46.9	Kaposi's sarcoma, unspecified
C48.0	Malignant neoplasm of retroperitoneum
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C49.0	Malignant neoplasm of connective and soft tissue of head, face and neck
C49.10	Malignant neoplasm of connective and soft tissue of unspecified upper limb, including shoulder
C49.11	Malignant neoplasm of connective and soft tissue of right upper limb including shoulder
C49.12	Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.20	Malignant neoplasm of connective and soft tissue of unspecified lower limb, including hip
C49.21	Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22	Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C49.3	Malignant neoplasm of connective and soft tissue of thorax
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.6	Malignant neoplasm of connective and soft tissue of trunk, unspecified
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola , unspecified male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast

C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
C51.0	Malignant neoplasm of labium majus
C51.1	Malignant neoplasm of labium minus
C51.2	Malignant neoplasm of clitoris
C51.8	Malignant neoplasm of overlapping sites of vulva
C53.0	Malignant neoplasm of endocervix
C53.1	Malignant neoplasm of exocervix
C53.8	Malignant neoplasm of overlapping sites of cervix uteri
C53.9	Malignant neoplasm of cervix uteri, unspecified
C54.0	Malignant neoplasm of isthmus uteri
C54.1	Malignant neoplasm of endometrium
C54.2	Malignant neoplasm of myometrium
C54.3	Malignant neoplasm of fundus uteri
C54.8	Malignant neoplasm of overlapping sites of corpus uteri
C54.9	Malignant neoplasm of corpus uteri, unspecified

C55	Malignant neoplasm of uterus, part unspecified
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.9	Malignant neoplasm of unspecified ovary
C57.00	Malignant neoplasm of unspecified fallopian tube
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C57.10	Malignant neoplasm of unspecified broad ligament
C57.11	Malignant neoplasm of right broad ligament
C57.12	Malignant neoplasm of left broad ligament
C57.20	Malignant neoplasm of unspecified round ligament
C57.21	Malignant neoplasm of right round ligament
C57.22	Malignant neoplasm of left round ligament
C57.3	Malignant neoplasm of parametrium
C57.4	Malignant neoplasm of uterine adnexa, unspecified
C57.7	Malignant neoplasm of other specified female genital organs
C57.8	Malignant neoplasm of overlapping sites of female genital organs
C57.9	Malignant neoplasm of female genital organ, unspecified
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
C70.0	Malignant neoplasm of cerebral meninges
C70.1	Malignant neoplasm of spinal meninges
C70.9	Malignant neoplasm of meninges, unspecified
C71.0	Malignant neoplasm of cerebrum, except lobes and ventricles
C71.1	Malignant neoplasm of frontal lobe
C71.2	Malignant neoplasm of temporal lobe
C71.3	Malignant neoplasm of parietal lobe
C71.4	Malignant neoplasm of occipital lobe
C71.5	Malignant neoplasm of cerebral ventricle
C71.6	Malignant neoplasm of cerebellum
C71.7	Malignant neoplasm of brain stem
C71.8	Malignant neoplasm of overlapping sites of brain
C71.9	Malignant neoplasm of brain, unspecified
C72.0	Malignant neoplasm of spinal cord
C72.9	Malignant neoplasm of central nervous system, unspecified
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C79.31	Secondary malignant neoplasm of brain
C79.32	Secondary malignant neoplasm of cerebral meninges

C79.89	Secondary malignant neoplasm of other specified sites
C79.9	Secondary malignant neoplasm of unspecified site
C83.30	Diffuse large B-cell lymphoma unspecified site
C83.31	Diffuse large B-cell lymphoma lymph nodes of head, face, and neck
C83.39	Diffuse large B-cell lymphoma extranodal and solid organ sites
C83.80	Other non-follicular lymphoma unspecified site
C83.81	Other non-follicular lymphoma lymph nodes of head, face, and neck
C83.89	Other non-follicular lymphoma extranodal and solid organ sites
D32.0	Benign neoplasm of cerebral meninges
D32.1	Benign neoplasm of spinal meninges
D32.9	Benign neoplasm of meninges, unspecified
D42.0	Neoplasm of uncertain behavior of cerebral meninges
D42.1	Neoplasm of uncertain behavior of spinal meninges
D42.9	Neoplasm of uncertain behavior of meninges, unspecified
D43.0	Neoplasm of uncertain behavior of brain, supratentorial
D43.1	Neoplasm of uncertain behavior of brain, infratentorial
D43.2	Neoplasm of uncertain behavior of brain, unspecified
D43.4	Neoplasm of uncertain behavior of spinal cord
I67.89	Other cerebrovascular disease
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.3	Personal history of malignant neoplasm of breast
Z85.43	Personal history of malignant neoplasm of ovary
Z80.49	Family history of malignant neoplasm of other genital organs
Z85.528	Personal history of other malignant neoplasm of kidney
Z85.831	Personal history of malignant neoplasm of soft tissue
Z85.841	Personal history of malignant neoplasm of brain
Z85.848	Personal history of malignant neoplasm of other parts of nervous tissue

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	11/20/2024	Annual Review: Updated Title of policy and combined with the Mvasi/Zirabev policy to make Bevacizumab. Retired policy MG.MM.PH.124 Mvasi/Zirabev. Updated dosage limits. Added statement: "For Medicare members – bevacizumab -please refer to our separate LCD/NCD Medicare criteria" Hepatocellular Carcinoma (HCC) Reworded: "The medication is used in combination with Tecentriq (atezolizumab intravenous infusion); AND Patient has not received prior systemic therapy" to: Used as first-line therapy in combination with atezolizumab; AND Patient has unresectable or metastatic disease †; OR Patient has liver-confined disease that is inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic disease; AND Patient has Child-Pugh Class A or B hepatic impairment; OR Patient has extensive liver tumor burden; AND Patient has Child-Pugh Class A or B hepatic impairment" Colorectal Cancer (CRC) † ‡ Removed: "Patient's disease is metastatic, unresectable, or advanced; AND Medication is not used as adjuvant treatment

		AND Used in combination with a fluoropyrimidine- (e.g., 5-fluorouracil/5-FU or capecitabine) or irinotecan-based regimen as first-line or subsequent therapy for metastatic, unresectable (or medically inoperable), or advanced disease; OR Used in combination with a fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin based regimen (not used first line) as second-line therapy for metastatic disease that has progressed on a first-line bevacizumab-containing regimen; OR Used in combination with trifluridine and tipiracil as subsequent therapy for advanced or metastatic disease after progression on all available regimens" Added: " Will not be used as part of adjuvant treatment; AND Used in combination with a fluoropyrimidine- (e.g., 5-fluorouracil/5-FU or capecitabine) based regimen as first-line or subsequent therapy for metastatic, unresectable (or medically inoperable), or advanced disease; AND Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; OR Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; AND Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy; OR Used in combination with irinotecan as initial treatment for unresectable metastatic disease; AND Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; AND Patient received previous FOLFOX or CapeOX within the past 12 months; OR Used in combination irinotecan as subsequent therapy for advanced or metastatic disease; AND Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; OR Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; AND Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy; OR Used in combination with a fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatinbased regimen (not used first line) as second-line therapy for metastatic disease that has progressed on a first-line bevacizumab-containing regimen †; OR Used in combination with trifluridine and tipiracil as subsequent therapy for advanced or metastatic disease; AND Patient progressed through all available regimens (e.g., oxaliplatin-based therapy, irinotecan-based therapy, fluoropyrimidine-based therapy, etc.)*; AND Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; OR Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; AND Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy; OR Used as primary treatment for T3, N Any; T1-2, N1-2; T4, N Any rectal cancer; AND Used in combination with a fluoropyrimidine- (e.g., 5-fluorouracil/5-FU or capecitabine) based regimen; AND Used if resection is contraindicated following total neoadjuvant therapy; AND Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; OR Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; AND Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy; OR Used if resection is contraindicated following neoadjuvant/definitive immunotherapy; AND Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease **Refer to NCCN Colon and Rectal Cancer guidelines for regimens."* Non-squamous non-small cell lung cancer (NSCLC) † ‡ Removed and reworded: "Patient's disease must be recurrent, unresectable, locally advanced, or metastatic; AND Used as first-line treatment in combination with carboplatin and paclitaxel OR The Patient meets ONE of the following criteria (a, b, c, or d): The tumor is positive for epidermal growth factor receptor (*EGFR*) exon 19 deletion or L858R mutations and bevacizumab is used in combination with erlotinib; OR

		The tumor is positive for one of the following mutations and bevacizumab is used in combination with other systemic therapies (i, ii,iii, iv, v, or vi):Epidermal growth factor receptor (*EGFR*) exon 20 mutation; OR *KRAS G12C* mutation; OR *BRAF V600E*; OR *NTRK1/2/3* gene fusion; OR *MET* exon 14 skipping mutation; OR *RET* rearrangement positive; OR Patient has previously received targeted drug therapy for an actionable mutation; OR The NSCLC tumor is negative or unknown for actionable mutations and the patient meets ONE of the following criteria (i or ii): Bevacizumab is used as initial therapy in combination with other systemic therapies; OR Bevacizumab is used as subsequent therapy" *Added: "*1. Used for recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease with no evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; AND Used as first-line therapy; AND Used in combination with erlotinib for EGFR exon 19 deletion or exon 21 L858R mutations; OR Used for one of the following: Patients with a performance status (PS) 0-1 who have tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) and PD-L1 expression < 1% PD-L1 expression positive (PD-L1 ≥ 1%) tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) Patients with a PS 0-1 who are positive for one of the following molecular biomarkers: EGFR exon 20, BRAF V600E, NTRK1/2/3 gene fusion, MET exon 14 skipping, RET rearrangement, or ERBB2 (HER2); AND Used in combination with one of the following: Carboplatin and paclitaxel † Pemetrexed AND either carboplatin or cisplatin in patients with contraindications¥ to PD-1 or PD-L1 inhibitors Atezolizumab, carboplatin, and paclitaxel; OR Used as subsequent therapy in patients with a PS 0-1; AND Used for one of the following: EGFR exon 19 deletion or exon 21 L858R mutation, EGFR S768I, L861Q, and/or G719X mutation, ALK rearrangement, or ROS1 rearrangement positive tumors AND patient received prior targeted therapy§ for those aberrations BRAF V600E mutation, NTRK1/2/3 gene fusion, MET exon 14 skipping mutation, or RET rearrangement positive tumors, PD-L1 expression positive (PD-L1 ≥ 1%) tumors that are negative for actionable molecular biomarkers* after prior PD-1/PD-L1 inhibitor therapy but no prior platinum-containing chemotherapy; AND Used in combination with one of the following: Carboplatin and paclitaxel in patients with contraindications¥ to PD-1 or PDL1 inhibitors, Pemetrexed AND either carboplatin or cisplatin in patients with contraindications¥ to PD-1 or PD-L1 inhibitors, Atezolizumab, carboplatin, and paclitaxel (excluding use in patients who have received prior PD-1/PD-L1 inhibitor therapy); OR Used as continuation maintenance therapy in patients who achieved a tumor response or stable disease after first-line systemic therapy; AND Used as a single agent (bevacizumab must have been included in the first-line regimen); OR Used in combination with pemetrexed following a first-line bevacizumab/pemetrexed/platinum chemotherapy regimen; OR Used in combination with atezolizumab following a first-line atezolizumab/carboplatin/paclitaxel/bevacizumab regimen; OR Used as continuation of therapy following disease progression on erlotinib with bevacizumab; AND Patient has asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited progression; AND Patient has T790M negative disease" Cervical Cancer † ‡ Removed and reworded: "Patient's disease must be persistent, recurrent, or metastatic; AND Used in combination with paclitaxel AND either cisplatin/carboplatin, or topotecan Added: "Disease has adenocarcinoma, adenosquamous, or squamous cell carcinoma histology; AND Patient has recurrent or metastatic disease; AND

		Used in combination with paclitaxel AND either cisplatin, carboplatin, or topotecan; OR Used in combination with pembrolizumab, paclitaxel, AND cisplatin or carboplatin; AND Tumor expresses PD-L1 (Combined Positive Score [CPS] ≥1) as determined by an FDA-approved or CLIA compliant test❖; OR Used as a single agent as subsequent therapy; OR Patient has small cell neuroendocrine carcinoma of the cervix (NECC); AND Patient has persistent, recurrent, or metastatic disease; AND Used in combination with paclitaxel and topotecan; OR Used as a single agent as subsequent therapy Renal cell carcinoma (RCC) Removed and reworded: "Patient has metastatic or relapsed disease; AND Must be used as a single agent for predominantly non-clear cell histology; OR Must be used in combination with interferon alfa; OR Used in combination with everolimus or erlotinib in patients with papillary or hereditary leiomyomatosis disease Added: " Used in combination with interferon alfa for metastatic disease †; OR Patient has relapsed or metastatic disease with non-clear cell histology; AND Used as a single agent ‡; OR Used in combination with everolimus ‡; OR Used in combination with erlotinib for advanced papillary disease including hereditary leiomyomatosis and renal cell carcinoma (HLRCC)-associated RCC ‡" Adult Central nervous system (CNS) cancer Removed: "Patient has tried at least one previous therapy; AND Patient has ONE of the following (a, b, c, d, e, f, g, h, or i):Anaplastic gliomas; OR Glioblastoma; OR Intracranial and spinal ependymoma (excluding subependymoma) in patient ≥ 18 years of age; OR Meningiomas; ORBrain, Spine, or Leptomeningeal metastases; OR Primary CNS lymphoma OR Medulloblastoma; OR Supratentorial Astrocytoma/Oligodendroglioma (Infiltrative, WHO Grade II); ORSymptoms due to one of the following (i, ii, or iii): Radiation necrosis; OR Poorly controlled vasogenic edema; OR Mass effect" Used as single-agent short-course therapy for symptom management related to radiation necrosis, poorly controlled vasogenic edema, or mass effect; AND Patient has a diagnosis of one of the following CNS cancers ‡: Circumscribed Glioma, Primary CNS Lymphoma, Meningiomas , Brain or Spine metastases, Medulloblastoma , Glioblastoma/Gliosarcoma/H3-mutated high-grade glioma , IDH-mutant Astrocytoma (WHO Grade 2-4) IDH-mutant, 1p19q codeleted Oligodendroglioma (WHO Grade 2 or 3) Intracranial or Spinal Ependymoma (excluding subependymoma); OR Used for recurrent or progressive disease; AND Patient has a diagnosis of one of the following CNS cancers: IDH-mutant, 1p19q codeleted Oligodendroglioma (WHO Grade 3) ‡ - Glioblastoma/Gliosarcoma/H3-mutated high-grade glioma †‡ - IDH-mutant Astrocytoma (WHO Grade 3 or 4) ‡; AND Used as a single agent; OR Used in combination with carmustine, lomustine, or temozolomide; AND Patient has failed bevacizumab monotherapy; OR Used as a single agent for Intracranial or Spinal Ependymoma (excluding subependymoma) after prior radiation therapy ‡; OR Used as a single agent for surgically inaccessible Meningiomas when radiation is not possible ‡ Ovarian cancer Fallopian Tube, and Primary Peritoneal Cancer † ‡ Φ

		Removed: " Patient has Stage II-IV ovarian cancer after primary surgery; ANDMedication is used in combination with carboplatin and paclitaxel followed by Avastin as a single agent; OR Patient has persistent or recurrent disease; AND (a or b)If patient is platinum sensitive, medication is used in combination with carboplatin AND one of the following: gemcitabine or paclitaxel; OR If patient is platinum resistant, medication is used in combination with one of the following: PEGylated liposomal doxorubicin, paclitaxel, or topotecan; OR Medication is used as single agent maintenance therapy if used previously as part of combination therapy in patients with a partial or complete remission following primary therapy or therapy for platinum-sensitive recurrence; OR Medication is used as neoadjuvant therapy in combination with paclitaxel and carboplatin; AND Patient has bulky stage III or IV disease or is a poor surgical candidate; OR Medication is used as adjuvant therapy in combination with paclitaxel and carboplatin; ANDPatient has stage II-IV disease; OR Patient has stage I-IV carcinosarcoma histologic disease" Added to update with: " Patient has malignant stage II-IV sex cord-stromal tumors ‡; AND Used as a single agent for clinically relapsed disease; OR Patient has epithelial* ovarian, fallopian tube, or primary peritoneal cancer †; AND Patient has persistent or recurrent disease; AND Bevacizumab has not been used previously; AND Patient is not experiencing an immediate biochemical relapse (i.e., rising CA-125 without radiographic evidence of disease); AND Patient has platinum-sensitive disease; AND Used as a single agent; OR Used in combination with carboplatin AND either gemcitabine, paclitaxel† or liposomal doxorubicin; OR Patient has platinum-resistant disease; AND Used as a single agent; OR Used in combination with one of the following: oral cyclophosphamide,gemcitabine, liposomal doxorubicin, paclitaxel, or topotecan; OR Used in combination with oral cyclophosphamide and pembrolizumab; OR Used in combination with mirvetuximab soravtansine-gynx (in folate receptor-alpha expressing tumors); OR Used in combination with carboplatin AND either gemcitabine, paclitaxel or liposomal doxorubicin; OR Used in combination with paclitaxel and carboplatin for rising CA-125 levels or clinical relapse in patients who have received no prior chemotherapy (mucinous, clear cell, carcinosarcoma, endometrioid, and high-grade serous histology only); OR Used in combination with paclitaxel and carboplatin for recurrence in patients who have received no prior chemotherapy (low-grade serous histology only); OR Used as maintenance therapy; AND Used for stage II-IV disease following primary therapy including bevacizumab; AND Used as a single agent in patients that are BRCA1/2 wild-type or unknown AND homologous recombination (HR) proficient, HR deficient, or status unknown(grade 2/3 endometrioid and high-grade serous histology only); OR Used in combination with olaparib or niraparib (if unable to tolerate olaparib); AND Patient is BRCA1/2 wild-type or unknown AND HR deficient (grade 2/3 endometrioid and high-grade serous histology only); OR Patient has a germline or somatic BRCA1/2 mutation (grade 2/3 endometrioid, high-grade serous, clear cell, carcinosarcoma histology only); OR Used as a single agent following recurrence therapy with chemotherapy plus bevacizumab for platinum-sensitive disease; OR

		Used as continued treatment for stable disease following neoadjuvant therapy (*endometrioid and serous histology only*); AND Used in combination with carboplatin AND paclitaxel or docetaxel; OR Used in combination with oxaliplatin and docetaxel; OR Used as neoadjuvant therapy (endometrioid and serous histology only); AND Used in combination with one of the following: Carboplatin AND paclitaxel or docetaxel Oxaliplatin and docetaxel; AND Patient is a poor surgical candidate or has a low likelihood of optimal cytoreduction; OR Used as adjuvant therapy; AND Used in combination with oxaliplatin and docetaxel; AND Patient has pathologic stage II-IV disease (mucinous, clear cell, carcinosarcoma,grade 2/3 endometrioid, and high-grade serous histology only); OR Used following interval debulking surgery (IDS) in patients with a response or stable disease to neoadjuvant therapy (endometrioid and serous histology only); AND Patient is a poor surgical candidate or has a low likelihood of optimal cytoreduction; OR Used in combination with carboplatin AND paclitaxel or docetaxel; AND Patient has pathologic stage II-IV disease; OR Used following interval debulking surgery (IDS) in patients with a response or stable disease to neoadjuvant therapy (endometrioid and serous histology only); AND Patient is a poor surgical candidate or has a low likelihood of optimal cytoreduction" Soft tissue Sarcoma ‡ Removed "or Hemangiopericytoma " From the following statement: "Used in combination with temozolomide for Solitary Fibrous Tumor or Hemangiopericytoma " Endometrial Carcinoma (Uterine Neoplasms) ‡ Removed and reworded the following: "Used as a single agent therapy for disease that has progressed on prior cytotoxic therapy; OR Used in combination with carboplatin and paclitaxel for advanced or recurrent disease" Added: "Patient has recurrent disease; AND Used as a single agent; AND Used as subsequent therapy for disease that has progressed on prior cytotoxic chemotherapy; OR Used as continuation maintenance therapy following use in combination with carboplatin and paclitaxel; OR Used in combination with carboplatin and paclitaxel" Malignant Pleural Mesothelioma (PM)‡ Removed: "Patient has unresectable or metastatic disease; AND One of the following applies (a, b, or c):Bevacizumab will be used in combination with a chemotherapy regimen; OR Bevacizumab will be used in combination with Tecentriq (atezolizumab intravenous infusion); OR Bevacizumab is being used as a single agent for maintenance therapy after the patient has received combination chemotherapy regimen" Added: " Used as first-line therapy; AND Used in combination with pemetrexed AND either cisplatin or carboplatin (if cisplatin ineligible); AND Patient has clinical stage I–IIIA disease with epithelioid histology; OR Patient has clinical stage IIIB or IV disease, sarcomatoid or biphasic histology, or medically inoperable disease; OR Used as subsequent therapy; AND Used in combination with pemetrexed AND either cisplatin or carboplatin (if cisplatin ineligible); AND Immunotherapy was administered as first-line treatment; OR Used as a rechallenge if pemetrexed-based treatment was administered first-line with good response" Removed Breast Cancer and AIDS-Related Kaposi Sarcoma indications. Updated procedure codes and NDCs. Updated Genomic Aberration chart.

EmblemHealth & ConnectiCare	04/21/2023	Added Vegzelma as non-preferred agent to criteria
EmblemHealth & ConnectiCare	9/14/2022	Under CNS Cancer – Removed. Used as a single agent OR in combination with one of the following: irinotecan, carmustine, lomustine, or temozolomide in patients with recurrent Glioblastomas † or Anaplastic Gliomas; OR 4. Medication is used as a single agent for progressive or recurrent Intracranial or Spinal Ependymoma (excluding subependymoma) after prior radiation therapy; OR 5. Medication is used as a single agent for patients with surgically inaccessible recurrent or progressive Meningioma when radiation is not possible
EmblemHealth & ConnectiCare	08/11/2022	Added Alymsys as non-preferred agent to Criteria
EmblemHealth & ConnectiCare	8/02/2022	Added Hepatocellular Carcinoma indication Under Colorectal Cancer – Added additional criteria "Used in combination with trifluridine and tipiracil as subsequent therapy for advanced or metastatic disease after progression on all available regimens" Under NSCLC criteria- removal of "Patient must have an ECOG performance status 0-2" and "Patient does not have locoregional recurrence without evidence of disseminated disease" Added – "The tumor is positive for epidermal growth factor receptor (EGFR) exon 19 deletion or L858R mutations and bevacizumab is used in combination with erlotinib" For Malignant Pleural Mesothelioma – added examples of chemotherapy regimens
EmblemHealth & ConnectiCare	07/28/2022	Updated Initial approval criteria: Must be prescribed by, or in consultation with an oncologist Updated Colorectal cancer, Cervical Cancer, RCC, CNS, Ovarian carcinoma Cancer to match FDA Label
EmblemHealth & ConnectiCare	3/24/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	12/20/2020	Clarifications: • Step therapy will apply to NEW starts only • NCCN-supported use (with 1 or 2A recommendation) will be covered Renewal criteria updated: • Removed: "Patient continues to meet criteria identified above" Added coverage: "Continuation of documented current and/or successful therapy with a non-preferred agent (Avastin)"
EmblemHealth & ConnectiCare	11/2/2020	Effective 01/01/2021 Member must fail trial of Mvasi AND Zirabev, prior to using Avastin (Medicare members are subject to this step therapy).
EmblemHealth & ConnectiCare	03/31/2020	Added to the Initial Criteria: Effective 07/01/2020, Mvasi and Zirabev are the preferred agents for Commercial and Medicaid members. Member must fail trial of Mvasi AND Zirabev, prior to using Avastin (Only Commercial and Medicaid members are subject to this step therapy). Initial Criteria: Added Patient is 18 years of age or older.

EmblemHealth & ConnectiCare	2/12/2019	Added Diagnosis Codes C51.0, C51.1, C51.2, C51.8

References

1. Avastin [package insert]. South San Francisco, CA; Genentech; June 2018. Accessed September 2019.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) bevacizumab. National Comprehensive Cancer Network, 2018. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed July 2018.
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