Clinical Policy: Bevacizumab (Alymsys, Avastin, Avzivi, Jobevne, Lytenava, Mvasi, Vegzelma, Zirabev)

Reference Number: CP.PHAR.93
Effective Date: 12.01.11
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Coding Implications
Revision Log

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

Description

Bevacizumab (Avastin®), its biosimilars [bevacizumab-maly (Alymsys®), bevacizumab-tnjn (Avzivi®), bevacizumab-nwgd (Jobevne™), bevacizumab-awwb (Mvasi®), bevacizumab-adcd (Vegzelma®), bevacizumab-bvzr (Zirabev™)], and bevacizumab-vikg (Lytenava™) are vascular endothelial growth factor-specific angiogenesis inhibitors.

FDA Approved Indication(s)

Avastin, Alymsys, Avzivi, Jobevne, Mvasi, Vegzelma, and Zirabev are indicated for the treatment of:

- Metastatic colorectal cancer (CRC), in combination with intravenous 5-fluorouracil (5-FU)-based chemotherapy for first- or second-line treatment
- Metastatic CRC, in combination 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
- Unresectable, locally advanced, recurrent, or metastatic non-squamous non-small cell lung cancer (NSCLC), in combination with carboplatin and paclitaxel for first-line treatment
- Recurrent glioblastoma in adults
- Metastatic renal cell carcinoma (RCC) in combination with interferon alfa
- Persistent, recurrent, or metastatic cervical cancer, in combination with paclitaxel and cisplatin, or paclitaxel and topotecan
- Epithelial ovarian, fallopian tube, or primary peritoneal cancer:
  - In combination with carboplatin and paclitaxel, followed by Avastin/Jobevne/Mvasi/Vegzelma/Zirabev as a single agent, for stage III or IV disease following initial surgical resection
  - In combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy regimens
  - In combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by Avastin/Jobevne/Mvasi/Vegzelma/Zirabev as a single agent, for platinum-sensitive recurrent disease
- Hepatocellular carcinoma (HCC) in combination with atezolizumab for patients with unresectable or metastatic HCC who have not yet received prior systemic therapy (*Avastin only*)

Lytenava is indicated for the treatment of neovascular (wet) age-related macular degeneration (nAMD).

Limitation(s) of use: Bevacizumab products are not indicated for adjuvant treatment of colon cancer.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that bevacizumab, Avastin, Alymsys, Avzivi, Jobevne, Lytenava, Mvasi, Vegzelma, and Zirabev are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Oncology - FDA-Approved Indications (must meet all)**:**

1. Request is for Avastin, Alymsys, Avzivi, Jobevne, Mvasi, Vegzelma, or Zirabev;
2. Diagnosis of one of the following (a-g):
   a. CRC;
   b. Non-squamous NSCLC;
   c. Glioblastoma (including gliosarcoma);
   d. RCC;
   e. Cervical cancer;
   f. Epithelial ovarian, fallopian tube, or primary peritoneal cancer;
   g. HCC;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Member meets one of the following (a-g):
   a. For CRC, both of the following (i and ii):
      i. Disease is advanced, metastatic, or unresectable;
      ii. Prescribed in combination with one of the following (1-5):
         1) 5-FU/leucovorin or capecitabine-based chemotherapy;
         2) FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin);
         3) Irinotecan or FOLFIRI (fluorouracil, leucovorin, and irinotecan);
         4) FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin);
         5) Lonsurf® if previously progressed through all available regimens;
   b. For non-squamous NSCLC, both of the following (i and ii):
      i. Disease is unresectable, recurrent, advanced, or metastatic;
      ii. Prescribed in one of the following ways (1-5):
         1) As single agent therapy;
         2) In combination with carboplatin and paclitaxel;
         3) In combination with pemetrexed with or without carboplatin or cisplatin;
         4) In combination with Tecentriq® with or without carboplatin and paclitaxel;
         5) In combination with erlotinib for sensitizing EGFR mutation-positive histology (i.e., EGFR exon 19 deletion or exon 21 L858R);
   c. For glioblastoma, member has recurrent disease or requires symptom management;

d. For RCC, both of the following (i and ii):
   i. Disease is relapsed or metastatic;
   ii. Prescribed in one of the following ways (1, 2, 3, or 4):
      1) As a single-agent;
      2) In combination with everolimus;
      3) In combination with interferon alfa;
      4) For advanced papillary RCC, including hereditary leiomyomatosis and renal cell carcinoma-associated RCC, only: In combination with erlotinib;
e. For cervical cancer, both of the following (i and ii):
   i. Disease is persistent, recurrent, or metastatic;
   ii. Prescribed in one of the following ways (1, 2, or 3):
      1) As a single agent;
      2) In combination with paclitaxel/cisplatin with or without Tecentriq, paclitaxel/carboplatin with or without Tecentriq, or paclitaxel/topotecan;
      3) In combination with Keytruda®, paclitaxel, and cisplatin/carboplatin for PD-L1-postive disease;
f. For epithelial ovarian, fallopian tube, or primary peritoneal cancer, prescribed in one of the following ways (i-vi):
   i. As a single agent;
   ii. In combination with a platinum agent (e.g., carboplatin, oxaliplatin) and chemotherapy (e.g., docetaxel, paclitaxel), followed by bevacizumab as a single agent;
   iii. For maintenance in combination with Lynparza® (or Zejula® if unable to tolerate Lynparza) for stage II-IV disease;
   iv. In combination with paclitaxel for small cell carcinoma (hypercalcemic type) recurrence therapy;
   v. For platinum-resistant persistent disease or recurrence, one of the following (1-5):
      1) In combination with paclitaxel, liposomal doxorubicin, topotecan, gemcitabine, or cyclophosphamide;
      2) In combination with carboplatin and paclitaxel, or carboplatin and gemcitabine, or carboplatin and liposomal doxorubicin, or FOLFIRI;
      3) In combination with cyclophosphamide and Keytruda, or paclitaxel and Keytruda;
      4) In combination with Ixempra® (if previously treated with a taxane);
      5) In combination with Elahere® (in folate receptor-alpha expressing tumors);
   vi. For platinum-sensitive persistent disease or recurrence, one of the following (1, 2, or 3):
      1) In combination with carboplatin and paclitaxel, or carboplatin and gemcitabine, or carboplatin and liposomal doxorubicin;
      2) In combination with Zejula as targeted therapy;
      3) In combination with Elahere in folate receptor-alpha expressing tumors;
g. For HCC, prescribed in combination with Tecentriq as one of the following (i or ii):
   i. First-line systemic therapy, and:
      1) Disease is unresectable or metastatic;

ii. Subsequent-line systemic therapy if progression on or after systemic therapy;

6. For Alymsys, Avastin, Avzivi, Jobevne, or Vegzelma requests, member meets one of the following (a or b):*
   **For Illinois HIM requests, the step therapy requirements below do not apply per IL HB 5395*
   a. Member must use Mvasi or Zirabev^, unless both are contraindicated or clinically significant adverse effects are experienced;
      ^Prior authorization may be required for Mvasi and Zirabev
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks (*see Appendix F for dose rounding guidelines*);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Oncology - Non-FDA-Approved Adult Indications (off-label) (must meet all)**:**
1. Request is for Avastin, Alymsys, Avzivi, Jobevne, Mvasi, Vegzelma, or Zirabev;
2. Diagnosis of one of the following conditions (a-j):
   a. Ampullary adenocarcinoma – intestinal type;
   b. Appendiceal neoplasms and cancers;
   c. One of the following types of central nervous system (CNS) cancers (i-viii):
      i. Glioma of one of the following types (1-4):
         1) Circumscribed glioma (e.g. glioma/glioneuronal tumors, pleomorphic xanthoastrocytoma[PXA]);
         2) High-grade glioma (PXA, high-grade astrocytoma with piloid features;
         3) IDH-mutant astrocytoma;
         4) Oligodendroglioma that is IDH-mutant, 1p19q codeleted;
      ii. Intracranial and spinal ependymoma;
      iii. Medulloblastoma;
      iv. Metastatic spine tumors or brain metastases;
      v. Meningioma;
      vi. Neurofibromatosis type 2 (NF2)-related schwannomas;
      vii. Primary CNS lymphoma;
      viii. Primary spinal cord tumors;
   d. Endometrial carcinoma;
   e. Peritoneal mesothelioma;
   f. Pleural mesothelioma;
   g. Small bowel adenocarcinoma;
   h. Soft tissue sarcoma – solitary fibrous tumor or angiosarcoma;
   i. Vaginal cancer;
   j. Vulvar cancer – adenocarcinoma or squamous cell carcinoma;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;

5. For Alymsys, Avastin, Avzivi, Jobevne, or Vegzelma requests, member meets one of the following (a or b):*
   **For Illinois HIM requests, the step therapy requirements below do not apply per IL HB 5395*
   a. Member must use Mvasi or Zirabev^, unless both are contraindicated or clinically significant adverse effects are experienced;
      ^Prior authorization may be required for Mvasi and Zirabev
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;
6. For ampullary adenocarcinoma, appendiceal neoplasms and cancers, peritoneal mesothelioma, pleural mesothelioma, small bowel adenocarcinoma, or vulvar cancer: Prescribed as part of combination therapy;
7. For NF2-related schwannomas: Prescribed as a single agent;
8. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 12 months or duration of request, whichever is less

C. Oncology - Non-FDA-Approved Pediatric Indications (off-label) (must meet all)**:**
1. Request is for Avastin, Alymsys, Avzivi, Jobevne, Mvasi, Vegzelma, or Zirabev;
2. Diagnosis of one of the following (a or b):
   a. Diffuse high-grade glioma;
   b. Medulloblastoma;
3. Prescribed by or in consultation with an oncologist;
4. Age < 18 years;
5. For Alymsys, Avastin, Avzivi, Jobevne, or Vegzelma requests, member meets one of the following (a or b):*
   **For Illinois HIM requests, the step therapy requirements below do not apply per IL HB 5395*
   a. Member must use Mvasi or Zirabev^, unless both are contraindicated or clinically significant adverse effects are experienced;
      ^Prior authorization may be required for Mvasi and Zirabev
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (*see Appendix E*);
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).**
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 12 months or duration of request, whichever is less

D. Ophthalmology (must meet all)**:**
1. Diagnosis of one of the following conditions (a-h):
   a. nAMD;
   b. Macular edema following retinal vein occlusion (RVO) (*off-label*);

c. Diabetic macular edema (DME) (*off-label*);
d. Diabetic retinopathy (DR) (*off-label*);
e. Neovascular glaucoma (*off-label*);
f. Choroidal neovascularization (including but not limited to choroidal neovascularization associated with: angioid streaks, no known cause, inflammatory conditions, high pathologic myopia, or ocular histoplasmosis syndrome, trauma, retinal dystrophies, rubeosis iridis, pseudoxanthoma elasticum) (*off-label*);
g. Radiation retinopathy (*off-label*);
h. Retinopathy of prematurity (ROP) (*off-label*);

2. Prescribed by or in consultation with an ophthalmologist;
3. Request is for bevacizumab intravitreal solution (e.g., Lytenava);
   **Requests for IV formulations of Avastin, Alymsys, Avzivi, Jobevne, Mvasi, Vegzelma, and Zirabev will not be approved*
4. Request meets one of the following (a, b, or c):
   a. For Lytenava for nAMD, dose does not exceed 1.25 mg every 28 days;
   b. For all other requests (*off-label*), dose does not exceed 1.25 mg per dose;
   c. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 12 months or duration of request, whichever is less

E. Other diagnoses/indications (must meet all)**:**

1. For Alymsys, Avastin, Avzivi, Jobevne, or Vegzelma requests for non-ophthalmology uses, member meets one of the following (a or b):*
   **For Illinois HIM requests, the step therapy requirements below do not apply per IL HB 5395*
   a. Member must use Mvasi or Zirabev^, unless both are contraindicated or clinically significant adverse effects are experienced;
      ^Prior authorization may be required for Mvasi and Zirabev
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;
2. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
3. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2 above does not apply, refer to the off-label use policy for the relevant line

of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Member meets one of the following (a, b, or c):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
   c. Documentation supports that member is currently receiving Alymsys, Avastin, Avzivi, Jobevne, Mvasi, Vegzelma, or Zirabev for a covered oncology indication listed in section I and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Alymsys, Avastin, Avzivi, Jobevne, or Vegzelma requests for non-ophthalmology uses, member meets one of the following (a or b):*
   **For Illinois HIM requests, the step therapy requirements below do not apply per IL HB 5395*
   a. Member must use Mvasi or Zirabev^, unless both are contraindicated or clinically adverse effects are experienced;
      ^Prior authorization may be required for Mvasi and Zirabev
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E*);
4. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. For Avastin, Alymsys, Avzivi, Jobevne, Mvasi, Vegzelma, or Zirabev, new dose does not exceed 15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks (*see Appendix F for dose rounding guidelines*);
   b. For Lytenava for nAMD, new dose does not exceed 1.25 mg every 28 days;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).
   **Prescribed chemotherapy regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 and either 2 or 3)**:**

1. For Alymsys, Avastin, Avzivi, Jobevne, or Vegzelma requests for non-ophthalmology uses, member meets one of the following (a or b):*
   **For Illinois HIM requests, the step therapy requirements below do not apply per IL HB 5395*
   a. Member must use Mvasi or Zirabev^, unless both are contraindicated or clinically significant adverse effects are experienced;
      ^Prior authorization may be required for Mvasi and Zirabev
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E);*
2. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or

3. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

5-FU: fluorouracil
CapeOX: capecitabine, oxaliplatin
CRC: colorectal cancer
DME: diabetic macular edema
DR: diabetic retinopathy
FDA: Food and Drug Administration
FOLFIRI: fluorouracil, leucovorin, irinotecan
FOLFIRINOX: fluorouracil, leucovorin, irinotecan, oxaliplatin
FOLFOX: fluorouracil, leucovorin, oxaliplatin
HCC: hepatocellular carcinoma
IDH: isocitrate dehydrogenase gene
IROX: irinotecan, oxaliplatin
nAMD: neovascular (wet) age-related macular degeneration
NCCN: National Comprehensive Cancer Network
NF2: neurofibromatosis type 2
NSCLC: non-small cell lung cancer
PD-L1: programmed death-ligand 1
PXA: pleomorphic xanthoastrocytoma
RCC: renal cell carcinoma
ROP: retinopathy of prematurity
RVO: retinal vein occlusion

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
HCC		
Examples of first-line systemic therapy: • Lenvima® (lenvatinib) • sorafenib (Nexavar®)	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): for Lytenava only:
  - Ocular or periocular infections
  - Active intraocular inflammation
  - Hypersensitivity
- Boxed warning(s): none reported

Appendix D: General Information

- 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 4% with NSCLC excluding predominant squamous histology. Patients with recent hemoptysis should not receive bevacizumab.

Appendix E: States with Regulations against Redirections in Cancer

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions.
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness.
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA.
IN	Yes	For advanced, metastatic cancer and associated conditions
LA	Yes[≠]	For stage 4 advanced, metastatic cancer or associated conditions. [≠]Exception if clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
MS	Yes	For advanced metastatic cancer and associated conditions
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	For stage 4 metastatic cancer and associated conditions
OK	Yes	For advanced metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes[^]	For cancer and associated conditions [^]Exception if step therapy is for AB-rated generic equivalent, interchangeable biological product, or biosimilar product to the equivalent brand drug
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

Appendix F: Dose Rounding Guidelines

Weight-based Dose Range	Vial Quantity Recommendation
≤ 104.99 mg	1 vial of 100 mg/4 mL
105 mg-209.99 mg	2 vials of 100 mg/4 mL
210 mg-314.99 mg	3 vials of 100 mg/4 mL
315 mg-419.99 mg	1 vial of 400 mg/16 mL

Weight-based Dose Range	Vial Quantity Recommendation
420 mg-524.99 mg	1 vial of 100 mg/4 mL and 1 vial of 400 mg/16 mL
525 mg-629.99 mg	2 vials of 100 mg/4 mL and 1 vial of 400 mg/16 mL
630 mg-734.99 mg	3 vials of 100 mg/4 mL and 1 vial of 400 mg/16 mL
735 mg-839.99 mg	2 vials of 400 mg/16 mL
840 mg-944.99 mg	1 vials of 100 mg/4 mL and 2 vials of 400 mg/16 mL
945 mg-1,049.99 mg	2 vials of 100 mg/4 mL and 2 vials of 400 mg/16 mL
1,050 mg-1,154.99 mg	3 vials of 100 mg/4 mL and 2 vials of 400 mg/16 mL
1,155 mg-1,259.99 mg	3 vials of 400 mg/16 mL
1,260 mg-1,364.99 mg	1 vials of 100 mg/4 mL and 3 vials of 400 mg/16 mL
1,365 mg-1,469.99 mg	2 vials of 100 mg/4 mL and 3 vials of 400 mg/16 mL
1,470 mg-1,574.99 mg	3 vials of 100 mg/4 mL and 3 vials of 400 mg/16 mL
1,575 mg-1,679.99 mg	4 vials of 400 mg/16 mL
1,680 mg-1,784.99 mg	1 vials of 100 mg/4 mL and 4 vials of 400 mg/16 mL
1,785 mg-1,889.99 mg	2 vials of 100 mg/4 mL and 4 vials of 400 mg/16 mL
1,890 mg-1,994.99 mg	3 vials of 100 mg/4 mL and 4 vials of 400 mg/16 mL
1,995 mg-2,099.99 mg	5 vials of 400 mg/16 mL

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Bevacizumab (Avastin), bevacizumab-maly (Alymsys), bevacizumab-tnjn (Avzivi), bevacizumab-nwgd (Jobevne), bevacizumab-awwb (Mvasi), bevacizumab-adcd (Vegzelma), bevacizumab-bvzr (Zirabev)	Metastatic CRC	5 mg/kg or 10 mg/kg IV every 2 weeks 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 product-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
	Recurrent glioblastoma	10 mg/kg IV every 2 weeks	10 mg/kg IV every 2 weeks
	Metastatic RCC	10 mg/kg IV every 2 weeks with interferon alfa	10 mg/kg IV every 2 weeks
	Persistent, recurrent, or metastatic cervical cancer	15 mg/kg IV every 3 weeks with paclitaxel and cisplatin or paclitaxel and topotecan	15 mg/kg IV every 3 weeks

Drug Name	Indication	Dosing Regimen	Maximum Dose
	Epithelial ovarian, fallopian tube, or primary peritoneal cancer	Stage III or IV disease following initial surgical resection 15 mg/kg IV every 3 weeks with carboplatin/paclitaxel for up to 6 cycles, followed by bevacizumab 15 mg/kg every 3 weeks as a single agent for a total of up to 22 cycles or until disease progression, whichever occurs earlier Platinum resistant 10 mg/kg IV every 2 weeks with weekly paclitaxel, pegylated liposomal doxorubicin, or topotecan 15 mg/kg IV every 3 weeks with topotecan Platinum sensitive 15 mg/kg IV every 3 weeks with carboplatin and paclitaxel (for 6 to 8 cycles) or with carboplatin and gemcitabine (for 6 to 10 cycles), followed by bevacizumab 15 mg/kg every 3 weeks as a single agent until disease progression	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks
	HCC	15 mg/kg IV every 3 weeks plus Tecentriq 1,200 mg IV on the same day, until disease progression or unacceptable toxicity	15 mg/kg IV every 3 weeks
	nAMD†, DME†, macular edema secondary to RVO†, neovascular glaucoma†	1.25 mg administered by intravitreal injection every 4 weeks	1.25 mg/dose
	DR†, choroidal neovascularization †, radiation retinopathy†	1.25 mg administered by intravitreal injection	1.25 mg/dose
	ROP†	0.2 mg administered by intravitreal injection	1.25 mg/dose
Bevacizumab-vikg (Lytenava)	nAMD	1.25 mg administered by intravitreal injection every month (approximately 28 days)	1.25 mg/dose

†Off-label

VI. Product Availability

Drug Name	Availability
Bevacizumab (Avastin), Bevacizumab-maly (Alymsys), Bevacizumab-tnjn (Avzivi), Bevacizumab-nwgd (Jobevne), Bevacizumab-awwb (Mvasi), Bevacizumab-adcd (Vegzelma), Bevacizumab-bvzr (Zirabev)	Single-use vials: 100 mg/4 mL, 400 mg/16 mL
Bevacizumab-vikg (Lytenava)	Single-dose vial for intravitreal injection: 1.25 mg (0.05 mL of 25 mg/mL)

VII. References

1. Avastin Prescribing Information. South San Francisco, CA: Genentech, Inc.; September 2022. Available at: www.avastin.com. Accessed August 6, 2026.
2. Alymsys Prescribing Information. Bridgewater, NJ: Amneal Pharmaceuticals, LLC; April 2022. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761231s000lbl.pdf. Accessed July 14, 2025.
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Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9257	Injection, bevacizumab, 0.25 mg
J9035	Injection, bevacizumab, 10 mg
J9999	Not otherwise classified, antineoplastic drugs
Q5107	Injection, bevacizumab-awwb, biosimilar, (Mvasi), 10 mg
Q5118	Injection, bevacizumab-bvcr, biosimilar, (Zirabev), 10 mg
Q5126	Injection, bevacizumab-maly, biosimilar, (Alymsys), 10 mg
Q5129	Injection, bevacizumab-adcd (Vegzelma), biosimilar, 10 mg
Q5160	Injection, bevacizumab-nwgd (jobevne), biosimilar, 10 mg

ICD-10-CM Diagnosis Codes that Support Coverage Criteria
The following is a list of diagnosis codes that support coverage for the applicable covered procedure code(s).

ICD-10-CM Code	Description
A18.53	Tuberculosis chorioretinitis
C17.0 – C17.9	Malignant neoplasm of small intestine
C18.0 – C18.9	Malignant neoplasm of colon
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 – C34.02	Malignant neoplasm of main bronchus
C34.10 – C34.12	Malignant neoplasm of upper lobe, bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30 – C34.32	Malignant neoplasm of lower lobe, bronchus or lung
C34.80 – C34.82	Malignant neoplasm of overlapping sites of bronchus and lung
C34.90 – C34.92	Malignant neoplasm of unspecified part of bronchus or lung
C48.0 – C48.8	Malignant neoplasm of retroperitoneum and peritoneum
C49.0 – C49.9	Malignant neoplasm of other connective and soft tissue
C50.01 – C50.929	Malignant neoplasm of breast
C53.0 – C53.9	Malignant neoplasm of cervix uteri
C54.0 – C55	Malignant neoplasm of corpus uteri
C56.1 – C56.9	Malignant neoplasm of ovary
C57.0 – C57.9	Malignant neoplasm of other and unspecified female genital organs
C64.1 – C64.9	Malignant neoplasm of kidney, except renal pelvis
C65.1 – C65.9	Malignant neoplasm of renal pelvis
C70.0 – C70.9	Malignant neoplasm of meninges
C71.0 – C71.9	Malignant neoplasm of brain

ICD-10-CM Code	Description
C72.0 – C72.9	Malignant of spinal cord, cranial neoplasm nerves and other parts of central nervous system
D32.0 – D32.9	Benign neoplasm of meninges
D42.0 – D42.9	Neoplasm of uncertain behavior of meninges
E08.311, E08.3211 – E08.3219, E08.3311 – E08.3319, E08.3411 – E08.3419, E08.3511 – E08.3519	Diabetes mellitus due to underlying condition with diabetic retinopathy with macular edema
E09.311, E09.3211 – E09.3219, E09.3311 – E09.3319, E09.3411 – E09.3419, E09.3511 – E093519	Drug or chemical induced diabetes mellitus with diabetic retinopathy with macular edema
E10.311, E10.3211 – E10.3219, E10.3311 – E10.3319, E10.3411 – E10.3419, E10.3511 – E10.3519	Type 1 diabetes mellitus with diabetic retinopathy with macular edema
E11.311, E11.3211 – E11.3219, E11.3311 – E11.3319, E11.3411 – E11.3419, E11.3511 – E11.3519	Type 2 diabetes mellitus with diabetic retinopathy with macular edema
E13.311, E13.3211 – E13.3219, E13.3311 – E13.3319, E13.3411 – E13.3419, E13.3511 – E13.3519	Other specified diabetes mellitus with diabetic retinopathy with macular edema
H16.401 – H16.449	Corneal neovascularization
H30.001 – H30.049	Focal chorioretinal inflammation
H30.101 – H30.139	Disseminated chorioretinal inflammation
H30.891 – H30.899	Other chorioretinal inflammations
H30.90 – H30.93	Unspecified chorioretinal inflammations
H32	Chorioretinal disorders in diseases classified elsewhere
H34.8110 – H 34.8192	Central retinal vein occlusion
H34.8310 – H34.8392	Tributary (branch) retinal vein occlusion
H35.051 – H35.059	Retinal neovascularization, unspecified
H35.141 – H35.169	Retinopathy of prematurity, stages 3 through 5
H35.3210 – H35.3293	Exudative age-related macular degeneration
H35.33	Angioid streaks of macula
H35.81	Retinal edema
H40.50X0-H40.53X4	Glaucoma secondary to other eye disorders [associated with vascular disorders of eye]
H44.20-H44.23	Degenerative myopia

ICD-10-CM Code	Description
H44.2A1-H44.2A9	Degenerative myopia with choroidal neovascularization
I67.89	Other cerebrovascular disease
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.048	Personal history of other malignant neoplasm of rectum, rectosigmoid junction, and anus
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
Z85.41	Personal history of malignant neoplasm of cervix uteri
Z85.42	Personal history of malignant neoplasm of other parts of uterus
Z85.43	Personal history of malignant neoplasm of ovary
Z85.44	Personal history of malignant neoplasm of other female genital organs
Z85.528	Personal history of other malignant neoplasm of kidney
Z85.53	Personal history of malignant neoplasm of renal pelvis
Z85.841	Personal history of malignant neoplasm of brain
Z85.848	Personal history of malignant neoplasm of other parts of nervous tissue

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2022 annual review: added additional NCCN-supported indications of ampullary adenocarcinoma cancer, malignant peritoneal mesothelioma, and pediatric diffuse high-grade glioma; re-classified anaplastic gliomas to astrocytoma and oligodendroglioma per updated NCCN classification; removed breast cancer indication, WHO grade 2 glioma indication, and single-agent therapy option for cervical cancer per NCCN; removed "radiographic and/or clinical relapse", "recurrent", and "carcinosarcoma with… BRCA 1/2 mutation" disease qualifiers for ovarian cancer as there are other clinical scenarios per NCCN; added new regimens for cervical cancer and CRC per NCCN; added legacy Wellcare line of business (WCG.CP.PHAR.93 to retire), aligned initial approval durations as 6 months, and aligned redirection to Mvasi or Zirabev; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section. Added HCPCS code [C9142]. RT4: added Vegzelma biosimilar to policy.	10.24.22	11.22
Updated HCPCS code: removed [C9142] and added [Q5126].	01.06.23	
Added HCPCS code [Q5129].	04.17.23	
Updated Appendix E to include Oklahoma.	06.07.23	
4Q 2023 annual review: per NCCN – for CRC added that disease is advanced, metastatic, or unresectable; for cervical cancer added option for single-agent therapy; for RCC removed combination	08.19.23	11.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
therapy option with interferon alfa; for ovarian cancers simplified bevacizumab combination therapy criterion when used with a platinum and chemotherapy along with corresponding staging update to IB-IV disease, added combination therapy option with gemcitabine for platinum-resistant disease, and removed combination therapy with Zejula; for HCC added Child-Pugh class B option; clarified off-label indication of primary central nervous system cancer is specifically for lymphoma; modified low-grade (WHO Grade I) glioma to circumscribed glioma; revised mesotheliomas to remove "malignant" per terminology change; references reviewed and updated.		
RT4: added newly FDA-approved biosimilar Avzivi to policy; for ovarian cancers, added combination therapy with Zejula per NCCN; created separate section for oncology – non-FDA-approved indications for pediatrics to include diffuse high-grade glioma.	12.14.23	
Updated Appendix E to include Mississippi.	06.05.24	
4Q 2024 annual review: re-organized FDA-approved indications for improved clarity; *for the following oncology indications, revised the following per NCCN*: for NSCLC, added qualifier of unresectable, specified sensitizing EGFR mutation for combination use with erlotinib, added additional agents with which pemetrexed and Tecentriq can be prescribed, removed requirement that the combination of carboplatin and paclitaxel is reserved for first-line treatment; for RCC, added qualifier of relapsed; for ovarian cancer, removed requirement that use with platinum agent + chemotherapy followed by single agent bevacizumab be limited to Stage IB-IV disease, added that combination with Zejula may be used for maintenance therapy if intolerant to Lynparza, added additional combination regimens for platinum-resistant disease (cyclophosphamide and Keytruda, Ixempra, Elahere), added combination with Elhere for platinum-sensitive disease; for HCC, removed requirement that disease is Child-Pugh class A or B and added pathway for adjuvant therapy in members at high risk of recurrence following resection or ablation; added additional off-label uses (pleomorphic xanthroastrocytoma, gliosarcoma, H3-mutated high-grade glioma, high-grade astrocytoma with piloid features, neurofibromatosis type 2 vestibular schwannomas with hearing loss, vaginal cancer); added requirement for combination use for ampullary adenocarcinoma, peritoneal mesothelioma, pleural mesothelioma, small bowel adenocarcinoma, or vulvar cancer; *for ophthalmology uses*: revised choroidal neovascularization to allow any cause and added additional examples, added radiation retinopathy and retinopathy of prematurity as supported by literature, added requirement for ophthalmologist prescriber, removed age restriction	08.12.24	11.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
as some covered diagnoses may affect pediatric populations; references reviewed and updated.		
RT4: added newly FDA-approved biosimilar Jobevne to criteria; for cervical cancer, added Tecentriq as an option to combination therapy for paclitaxel/cisplatin and paclitaxel/carboplatin, and clarified topotecan is used with paclitaxel per NCCN; for HCC, removed option for use as adjuvant therapy following resection or ablation and member is at high risk for recurrence and added option for use as subsequent-line systemic therapy if progression on or after systemic therapy per NCCN.	05.05.25	
Updated Appendix E with revised language and exception for Tennessee.	05.14.25	
4Q 2025 annual review: for all indications, added step therapy bypass for IL HIM per IL HB 5395, extended initial approval duration for Medicaid and HIM from 6 months to 12 months for this maintenance medication for a chronic condition; *for the following oncology indications, revised the following per NCCN*: for epithelial ovarian, fallopian tube, and primary peritoneal cancer, added option for combination use in platinum-resistant persistent disease with carboplatin and paclitaxel, carboplatin and gemcitabine, or carboplatin and liposomal doxorubicin; added additional off-label use in primary spinal cord tumors; *for ophthalmology uses*, revised diabetic retinopathy to allow any cause and stage; references reviewed and updated.	07.30.25	11.25
HCPCS code added [Q5160].	01.06.26	
Updated Appendix E to include Indiana.	03.26.26	
4Q 2026 annual review: added ICHRA line of business; updated Appendix E with revised language for Tennessee; for RCC, added option for use in combination with interferon alfa per FDA label; *for the following oncology indications, revised the following per NCCN:* added use in appendiceal neoplasms and cancers, clarified glioblastoma includes gliosarcoma, added use in NF2-related schwannomas, removed prescribed by in combination with IROX for CRC, for epithelial ovarian, fallopian tube, and primary peritoneal cancer, added use in combination with paclitaxel for small cell carcinoma (hypercalcemic type) recurrence therapy, added use in combination with FOLFIRI for platinum-resistant disease, added use in combination with paclitaxel and Keytruda for platinum-resistant disease; *for ophthalmology uses*, revised maximum dose for off-label uses to 1.25 mg per AAO guidelines and Clinical Pharmacology; RT4: added newly approved intravitreal formulation Lytenava for nAMD; separated FDA approved indication sections into oncology indications and ophthalmology indications; for oncology indications,	08.06.26	11.26

Reviews, Revisions, and Approvals	Date	P&T Approval Date
added criterion that request is for Avastin, Alymsys, Avzivi, Jobevne, Mvasi, Vegzelma, or Zirabev; references reviewed and updated.		

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.

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