

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

Reference Number: LA.PHAR.93

Effective Date: 04.21

Last Review Date: ~~06.17.25~~ 01.26.26

Line of Business: Medicaid

[Coding Implications](#)
[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description

Bevacizumab (Avastin®) and its biosimilars [bevacizumab-maly (Alymsys®), bevacizumab-tnjn (Avzivi®), bevacizumab-nwgd (Jobevne™), bevacizumab-awwb (Mvasi®), bevacizumab-adcd (Vegzelma™), bevacizumab-bvzr (Zirabev™)] 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

Avastin is also indicated for the treatment of:

- Hepatocellular carcinoma (HCC) in combination with atezolizumab for patients with unresectable or metastatic HCC who have not yet received prior systemic therapy.

Commented [JL1]: Removed Alymsys

The PI for Alymsys and Avzivi does not list the following combination

- In combination with carboplatin and paclitaxel, followed by XX as a single agent, for stage III or IV disease following initial surgical resection
- The combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by XX as a single agent, for platinum-sensitive recurrent disease

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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 Louisiana Healthcare Connections that Avastin, Alymsys, Avzivi, Jobevne, Mvasi, Vegzelma, and Zirabev are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of one of the following (a-g):
 - a. CRC;
 - b. Non-squamous NSCLC;
 - c. Glioblastoma;
 - d. RCC;
 - e. Cervical cancer;
 - f. Epithelial ovarian, fallopian tube, or primary peritoneal cancer;
 - g. HCC;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. 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 (1-6):
 - 1) 5-FU/leucovorin or capecitabine-based chemotherapy;
 - 2) IROX (irinotecan and oxaliplatin);
 - 3) FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin);
 - 4) Irinotecan or FOLFIRI (fluorouracil, leucovorin, and irinotecan);
 - 5) FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin);
 - 6) Lonsurif[®] 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;

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- 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, or 3):
 - 1) As a single-agent;
 - 2) In combination with everolimus;
 - 3) 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-positive disease;
- f. For epithelial ovarian, fallopian tube, or primary peritoneal cancer, prescribed in one of the following ways (i-v):
 - 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. For platinum-resistant persistent disease or recurrence: ~~In combination with paclitaxel, liposomal doxorubicin, topotecan, gemcitabine, cyclophosphamide, cyclophosphamide and Keytruda, Ixempra® (if previously treated with a taxane), or Elahere™ (in folate receptor alpha expressing tumors); one of the following (1-5):~~
 - v. ~~For platinum-sensitive persistent disease or recurrence (1, 2, or 3):~~
 - 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;~~
 - 3) ~~In combination with cyclophosphamide and Keytruda;~~
 - 4) ~~In combination with Ixempra® (if previously treated with a taxane);~~
 - 5) ~~In combination with Elahere® (in folate receptor-alpha expressing tumors);~~
 - v. ~~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;

Commented [JL2]: Removed during 4A23 AR due to change in status to 2B recommendation.

However, added back in since the cancer is an FDA approved indication to prevent PA going through off-label route and subsequently overturned/ approved since it is NCCN recommended

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- ii. Subsequent-line systemic therapy if progression on or after systemic therapy;
- ~~5.~~ For Alymsys, Avastin, Avzivi, Jobevne, or Vegzelma requests, member ~~meets one of the following (a or b):~~
- ~~a.~~ ~~5.~~ 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. 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-E~~ 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: ~~6~~12 months

B. Oncology - Non-FDA-Approved Adult Indications (off-label) (must meet all):

- 1. Diagnosis of one of the following conditions (a-~~op~~):
 - a. Glioma of one of the following types (i-vii):
 - i. Oligodendroglioma that is IDH-mutant, 1p19q codeleted;
 - ii. IDH-mutant astrocytoma;
 - iii. Circumscribed glioma;
 - iv. Pleomorphic xanthroastrocytoma;
 - v. Gliosarcoma;
 - vi. H3-mutated high-grade glioma;
 - vii. High-grade astrocytoma with piloid features;
 - b. Ampullary adenocarcinoma – intestinal type;
 - c. Endometrial carcinoma;
 - d. Intracranial and spinal ependymoma;
 - e. Peritoneal mesothelioma;
 - f. Pleural mesothelioma;
 - g. Medulloblastoma;
 - h. Meningioma;
 - i. Metastatic spine tumors or brain metastases;
 - j. Primary central nervous system lymphoma;
 - ~~k.~~ k. Primary spinal cord tumors;
 - ~~l.~~ l. Small bowel adenocarcinoma;
 - ~~m.~~ m. Soft tissue sarcoma – solitary fibrous tumor or angiosarcoma;
 - ~~n.~~ n. Vulvar cancer – adenocarcinoma or squamous cell carcinoma;
 - ~~o.~~ o. Neurofibromatosis type 2 vestibular schwannomas with hearing loss;
 - ~~p.~~ p. Vaginal cancer;
- 2. Prescribed by or in consultation with an oncologist;
- 3. Age ≥ 18 years;
- 4. For Alymsys, Avastin, Avzivi, Jobevne, or Vegzelma requests, member meets one of the following (a or b):
 - a. Member must use Mvasi or Zirabev[^] unless both are contraindicated or clinically significant adverse effects are experienced;^{*}

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**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*);
- 5. For ampullary adenocarcinoma, peritoneal mesothelioma, pleural mesothelioma, small bowel adenocarcinoma, or vulvar cancer: Prescribed as part of combination therapy;
- 6. For neurofibromatosis type 2 vestibular schwannomas with hearing loss: Prescribed as a single agent;
- 7. 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: 6-12 months

C. Oncology - Non-FDA-Approved Pediatric Indications (off-label) (must meet all):

- 1. Diagnosis of one of the following (a or b):
 - a. Diffuse high-grade glioma;
 - b. Medulloblastoma;
- 2. Prescribed by or in consultation with an oncologist;
- 3. Age < 18 years;
- 4. For Alymsys, Avastin, Avzivi, Jobevne, or Vegzelma requests, member meets one of the following (a or b):
 - a. ~~Member 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);~~
- 5. 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: 6-12 months

D. Ophthalmology - Non-FDA-Approved Indications (off-label) (must meet all):

- 1. Diagnosis of one of the following conditions (a-g):
 - a. Neovascular (wet) age-related macular degeneration; (nAMD);
 - b. Macular edema following retinal vein occlusion; (RVO);
 - c. Diabetic macular edema; (DME);
 - d. ~~Proliferative diabetic~~Diabetic retinopathy; (DR);
 - e. Neovascular glaucoma;
 - 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);
 - g. ~~Diabetic retinopathy associated with ocular neovascularization (choroidal, retinal, iris);~~

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~~h.g.~~ Radiation retinopathy;

~~i.h.~~ Retinopathy of prematurity (ROP);

2. Prescribed by or in consultation with an ophthalmologist;
3. Request is for bevacizumab intravitreal solution;
**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 or b):
 - a. Dose does not exceed 2.5 mg per dose;
 - b. 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: ~~6~~12 months

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):~~

~~a. 1.~~ ~~Member must 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*

~~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 ~~LA.PMN.255~~.

~~2.~~ LA.PMN.255

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 LA.PMN.53

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II. Continued Therapy

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

1. ~~Member meets one of the following (a or b):~~

~~a.~~ Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;

~~b.~~ 2. 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.~~ 3. Member is responding positively to therapy;

~~3.~~ ~~4.~~ For Alymsys, Avastin, Avzivi, Jobevne, or Vegzelma requests for non-ophthalmology uses, member ~~meets one of the following (a or b):~~

~~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.~~ 5. If request is for a dose increase, request meets one of the following (a or b):*

~~a.~~ a. New dose does not exceed 15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks (*see Appendix F-E for dose rounding guidelines*);

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~~b.~~ b. 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: 6 months

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):~~

~~a. 1. Member~~ must use Mvasi or Zirabev, ^A unless both are contraindicated or clinically significant adverse effects are experienced;*

^Δ**Prior authorization may be required for Mvasi and Zirabev*

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 LA.PMN.255

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 LA.PMN.53

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

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy LA.PMN.53

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

NSCLC: non-small cell lung cancer

PD-L1: programmed death-ligand 1

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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<u>Metastatic carcinoma of the colon or rectum</u>		

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
FOLFOX4 = Infusional 5-FU/leucovorin/ oxaliplatin	Oxaliplatin 85 mg/m ² IV over 2 hours day 1; leucovorin 200 mg/m ² IV over 2 hours days 1 & 2, followed by 5-FU 400 mg/m ² IV bolus over 2-4 minutes, followed by 600 mg/m ² IV 5-FU continuous infusion over 22 hours on days 1 & 2. Repeat cycle every 14 days.	Varies
FOLFIRI = Infusional 5-FU/ leucovorin/Camptosar [®] (irinotecan)	Camptosar 180 mg/m ² IV over 90 minutes day 1; Leucovorin 400 mg/m ² IV over 2 hours day 1 followed by 5-FU 400 mg/m ² IV bolus over 2-4 minutes, followed by 2.4 gm/m ² IV 5-FU continuous infusion over 46 hours. Repeat cycle every 14 days.	Varies
capecitabine (Xeloda [®])	2500 mg/m ² PO BID for 2 weeks; repeat cycles of 2 weeks on and 1 week off. For patients who cannot tolerate intensive therapy.	Varies
IROX = oxaliplatin/Camptosar (irinotecan)	Oxaliplatin 85 mg/m ² IV followed by Camptosar 200 mg/m ² IV over 30-90 minutes every 3 weeks	Varies
Camptosar (irinotecan)	180 mg/m ² IV every 2 weeks or 300-350 mg/m ² IV every 3 weeks	Varies
Lonsurf [®] (trifluridine and tipiracil)	35 mg/m ² (based on trifluridine component) PO BID on days 1-5 and 8-12, repeated every 28 days	Trifluridine 80 mg/dose
NSCLC		
Examples of drugs used in single- or multi-drug chemotherapy regimens: • Cisplatin, carboplatin, paclitaxel, docetaxel, vinorelbine, gemcitabine, etoposide, irinotecan, vinblastine, mitomycin, ifosfamide, pemetrexed disodium, (Alimta [®]) erlotinib (Tarcova [®]), Tecentriq [®] (atezolizumab)	Various doses	Varies
Ovarian Cancer		
Examples of drugs used in single-	Various doses	Varies

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
or multi-drug chemotherapy regimens: • carboplatin and paclitaxel, docetaxel and carboplatin, Lynparza® (olaparib);		
<i>Glioblastoma Multiforme</i>		
temozolomide (Temodar®)	Maintenance phase cycles: 150 mg–200 mg/m ² PO days 1–5. Repeat every 28 days.	Varies
carmustine (Bienu®)	150 mg to 200 mg/m ² IV on day 1. Repeat every 6–8 weeks for one year or tumor progression.	Varies
<i>Cervical Cancer</i>		
Examples of drugs used in multi-drug chemotherapy regimens: • cisplatin/paclitaxel with or without Tecentriq®; carboplatin/paclitaxel with or without Tecentriq®; cisplatin/topotecan (Hycamtin®); topotecan/paclitaxel	Various doses	Varies
<i>HCC</i>		
Example of drugs used in multi-drug chemotherapy regimens: tremelimumab act1 + durvalumab Examples of first-line systemic therapy: • Lenvima® (lenvatinib) • sorafenib (Nexavar®)	Various doses	Varies

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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
 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 2.3%–4% with NSCLC excluding predominant squamous histology. Patients with recent hemoptysis should not receive bevacizumab.

Appendix E: States with Regulations against Redirections in Certain Oncology Settings

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State	Step-Therapy Prohibited?	Notes
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.

Appendix EF: 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
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

Indication	Dosing Regimen	Maximum Dose
Metastatic CRC	5 mg/kg or 10 mg/kg once IV every 14 days <u>2 weeks</u> as an IV infusion in combination with a 5-FU based chemotherapy regimen until disease progression is detected.	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks
	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 <u>Avastin</u> bevacizumab product-containing	

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Indication	Dosing Regimen	Maximum Dose
	regimen	
Non-squamous NSCLC	15 mg/kg IV infusion every 3 weeks with carboplatin/paclitaxel	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks
Recurrent glioblastoma	10 mg/kg IV every 2 weeks	10 mg/kg IV every 2 weeks
Ovarian cancer, stage III or IV disease following initial surgical resection Metastatic RCC	15 mg/kg IV infusion every 3 weeks with carboplatin/paclitaxel for up to 6 cycles, followed by bevacizumab 15 mg/kg every 3 weeks as a single agent interferon alfa	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks
Persistent, recurrent, or metastatic cervical cancer Platinum resistant ovarian cancer	15 mg/kg intravenously IV every 3 weeks with weekly paclitaxel, liposomal doxorubicin, and cisplatin or paclitaxel and topotecan	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks
Epithelial sensitive ovarian, fallopian tube, or primary peritoneal cancer Platinum sensitive	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 intravenously 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 Teentriq 1,200 mg IV on the same day	15 mg/kg IV every 3 weeks

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CLINICAL POLICY
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Indication	Dosing Regimen	Maximum Dose
Clear cell renal carcinoma	10 mg/kg IV every 2 weeks with interferon alfa	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks
Glioblastoma multiforme, anaplastic astrocytoma, anaplastic oligodendroglioma	10 mg/kg IV every 2 weeks	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks
Soft tissue sarcoma	15 mg/kg IV infusion every 3 weeks	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks
Cervical cancer HCC	15 mg/kg IV infusion every 3 weeks (in combination with paclitaxel and either cisplatin or topotecan) plus Tecentriq 1,200 mg IV on the same day, until disease progression or unacceptable toxicity.	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks
Neovascular (wet) macular degeneration	1.25 to 2.5 mg administered by intravitreal injection every 4 weeks	2.5 mg/dose
Neovascular glaucoma	1.25 mg administered by intravitreal injection every 4 weeks	2.5 mg/dose
Macular AMD [†] , DME [†] , macular edema secondary to retinal vein occlusion RVO [†] , neovascular glaucoma [†]	1 mg to 2.5 mg administered by intravitreal injection every 4 weeks	2.5 mg/dose
Proliferative diabetic DR [†] , choroidal neovascularization [†] , radiation retinopathy [†]	1.25 mg administered by intravitreal injection 5 to 20 days before vitrectomy	2.5 mg/dose
Diabetic macular edema ROP [†]	1.25 to 2 mg administered by intravitreal injection	2.5 mg/dose

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Indication	Dosing Regimen	Maximum Dose
Malignant mesothelioma of pleura	15 mg/kg IV (plus pemetrexed 500 mg/m ² IV and cisplatin 75 mg/m ² IV) every 21 days for up to 6 cycles, followed by maintenance bevacizumab 15 mg/kg every 21 days until disease progression or unacceptable toxicity. All patients should receive folic acid 400 mcg orally daily and vitamin B12 1000 mcg IM every 3 weeks, both beginning 7 days prior to pemetrexed and continuing for 3 weeks following the last pemetrexed dose (off-label dosage).	2.5 mg/dose
Metastatic CRC in previously untreated elderly patients ineligible for oxaliplatin or irinotecan-based chemotherapy	7.5 mg/kg IV on day 1 with capecitabine 1,000 mg/m ² orally twice daily on days 1 to 14, given every 3 weeks until disease progression.	15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks

[†]Off-label

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VI. Product Availability

Single-use vials: 100 mg/4 mL, 400 mg/16 mL

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Oncology

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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.

Commented [JL4]: HCPCS code unavailable for Avzivi

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

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ICD-10-CM Code	Description
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
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 – E09.3519	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

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ICD-10-CM Code	Description
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
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	LDH Approval Date
Converted corporate to local policy	01.21	04.21
FDA indication language updated for Zirabev to reflect expansion of indication to include epithelial ovarian, fallopian tube, or primary peritoneal cancer; amended language for ophthalmology non-FDA approved indications to be: request is for bevacizumab intravitreal solution; Applied redirection of Avastin to preferred biosimilars to other diagnoses/indications; Added additional NCCN-supported regimens and classifications for colorectal cancer, NSCLC, glioblastoma, cervical cancer, and epithelial ovarian, fallopian tube, or	04.22	07.23.22

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Reviews, Revisions, and Approvals	Date	LDH Approval Date
primary peritoneal cancer; added criterion that HCC be classified as Child-Pugh class A disease per NCCN; added low-grade WHO grade I glioma to NCCN-supported off-label indication; Updated with Mvasi's FDA-approved indications of epithelial ovarian, fallopian tube, or primary peritoneal cancers.		
Added newly FDA-approved biosimilar Alysms to policy; generalized language for oncology redirection bypass. 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 and colorectal cancers per NCCN; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section. Added HCPCS codes C9142, Q5126, Q5129. Added Vegzelma biosimilar to policy. Added blurb this policy is for medical benefit only.	06.27.23	01.03.24
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 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; 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.	05.07.24	07.29.24
Removal of Appendix E, as LDH previously advised it is not applicable to Medicaid. Fe-organized FDA-approved indications for improved clarity; <i>for the following oncology indications, revised the following per NCCN:</i> for NSCLC, added qualifier of unresectable,	01.15.25	04.07.25

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Reviews, Revisions, and Approvals	Date	LDH Approval Date
<p>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; <i>for ophthalmology uses</i>: 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 as some covered diagnoses may affect pediatric populations; references reviewed and updated.</p>		
<p>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.</p>	06.17.25	11.06.25
<p><u>Extended initial approval duration 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</u></p>	01.26.26	

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Reviews, Revisions, and Approvals	Date	LDH Approval Date
<u>diabetic retinopathy to allow any cause and stage; references reviewed and updated. HCPCS code added [Q5160].</u>		

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. LHCC 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.

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 LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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.

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Bevacizumab and Biosimilars



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