

## SPECIALTY GUIDELINE MANAGEMENT

### AVASTIN (bevacizumab) MVASI (bevacizumab-awwb) ZIRABEV (bevacizumab-bvzr)

#### POLICY

#### I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

##### A. FDA-Approved Indications

1. **Metastatic colorectal cancer (mCRC)**
  - a. Avastin, Mvasi, or Zirabev, in combination with intravenous fluorouracil-based chemotherapy, is indicated for the first- or second-line treatment of patients with metastatic colorectal cancer.
  - b. Avastin, Mvasi, or Zirabev, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy, is indicated for the second-line treatment of patients with metastatic colorectal cancer who have progressed on a first-line bevacizumab-containing regimen.
2. **First-line non-squamous non-small cell lung cancer (NSCLC)**  
Avastin, Mvasi, or Zirabev, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer.
3. **Recurrent glioblastoma (RGM)**  
Avastin, Mvasi, or Zirabev, is indicated for the treatment of recurrent glioblastoma in adults.
4. **Metastatic renal cell carcinoma (mRCC)**  
Avastin, Mvasi, or Zirabev, in combination with interferon alfa, is indicated for the treatment of metastatic renal cell carcinoma.
5. **Persistent, recurrent, or metastatic cervical cancer**  
Avastin, Mvasi, or Zirabev, in combination with paclitaxel and cisplatin or paclitaxel and topotecan, is indicated for the treatment of patients with persistent, recurrent, or metastatic cervical cancer.
6. **Epithelial ovarian, fallopian tube, or primary peritoneal cancer**
  - a. Avastin, in combination with carboplatin and paclitaxel, followed by Avastin as a single agent, is indicated for the treatment of patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection.
  - b. Avastin, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan, is indicated for the treatment of patients with platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer who received no more than 2 prior chemotherapy regimens.
  - c. Avastin, in combination with carboplatin and paclitaxel, or with carboplatin and gemcitabine, followed by Avastin as a single agent, is indicated for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.

##### B. Compendial Uses

1. Breast cancer for recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-negative disease
2. Central nervous system (CNS) cancers
  - a. Low-grade (WHO Grade II) infiltrative supratentorial astrocytoma/oligodendroglioma
  - b. Intracranial and spinal ependymoma (excluding subependymoma)
  - c. Anaplastic gliomas
  - d. Medulloblastoma

Reference number(s)
1891-A

- e. Primary central nervous system lymphoma
- f. Meningiomas
- g. Limited and extensive brain metastases
- h. Leptomeningeal metastases
- i. Metastatic spine tumors
- 3. Malignant pleural mesothelioma
- 4. Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer
  - a. Carcinosarcoma (malignant mixed Müllerian tumors)
  - b. Clear cell carcinoma
  - c. Mucinous carcinoma
  - d. Grade 1 endometrioid carcinoma
  - e. Low-grade serous carcinoma
  - f. Ovarian borderline epithelial tumors (low malignant potential) with invasive implants
  - g. Malignant sex cord-stromal tumors
- 5. Soft tissue sarcoma
  - a. Angiosarcoma
  - b. Solitary fibrous tumor/Hemangiopericytoma
- 6. AIDS-related Kaposi sarcoma
- 7. Uterine/Endometrial cancer
- 8. Vulvar cancer
- 9. Peritoneal mesothelioma
- 10. Pericardial mesothelioma
- 11. Tunica vaginalis testis mesothelioma
- 12. Small bowel adenocarcinoma
- 13. Appendiceal carcinoma
- 14. Anal adenocarcinoma
- 15. Ophthalmic disorders
  - a. Diabetic macular edema
  - b. Neovascular (wet) age-related macular degeneration (AMD)
  - c. Macular edema following retinal vein occlusion (RVO)
  - d. Proliferative diabetic retinopathy
  - e. Choroidal neovascularization (CNV)
  - f. Neovascular glaucoma; adjunct
  - g. Retinopathy of prematurity
  - h. Polypoidal choroidal vasculopathy

All other indications are considered experimental/investigational and not medically necessary.

## II. CRITERIA FOR INITIAL APPROVAL

### A. Ophthalmic disorders

Authorization of 6 months may be granted for treatment of the following retinal disorders:

- 1. Diabetic macular edema
- 2. Neovascular (wet) age-related macular degeneration
- 3. Macular edema following retinal vein occlusion
- 4. Proliferative diabetic retinopathy
- 5. Choroidal neovascularization (including myopic choroidal neovascularization, angioid streaks, choroiditis [including choroiditis secondary to ocular histoplasmosis], idiopathic degenerative myopia, retinal dystrophies, rubeosis iridis, pseudoxanthoma elasticum, and trauma)
- 6. Neovascular glaucoma
- 7. Retinopathy of prematurity
- 8. Polypoidal choroidal vasculopathy

**B. Colorectal cancer (CRC)**

Authorization of 12 months may be granted for treatment of colorectal cancer, including small bowel adenocarcinoma, appendiceal carcinoma, and anal adenocarcinoma.

**C. Non-small cell lung cancer (NSCLC)**

Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic non-squamous NSCLC.

**D. CNS cancer**

Authorization of 12 months may be granted for treatment of the following types of CNS cancer:

1. Glioblastoma
2. Intracranial and spinal ependymoma (excludes subependymoma)
3. Anaplastic gliomas
4. Low-grade (WHO Grade II) infiltrative supratentorial astrocytoma/oligodendroglioma
5. Medulloblastoma
6. Primary central nervous system lymphoma
7. Meningiomas
8. Limited and extensive brain metastases
9. Leptomeningeal metastases
10. Metastatic spine tumors

**E. Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer**

Authorization of 12 months may be granted for treatment of the following types of ovarian cancer, fallopian tube cancer, and primary peritoneal cancer:

1. Epithelial ovarian cancer, including:
  - i. Carcinosarcoma (malignant mixed Müllerian tumors)
  - ii. Clear cell carcinoma
  - iii. Mucinous carcinoma
  - iv. Grade 1 endometrioid carcinoma
  - v. Low-grade serous carcinoma
  - vi. Borderline epithelial tumors (low malignant potential) with invasive implants
  - vii. Malignant sex cord-stromal tumors
2. Fallopian tube cancer
3. Primary peritoneal cancer

**F. Uterine/Endometrial cancer**

Authorization of 12 months may be granted for treatment of progressive, advanced, or recurrent uterine cancer or endometrial cancer.

**G. Cervical/Vaginal cancer**

Authorization of 12 months may be granted for treatment of persistent, recurrent, or metastatic cervical or vaginal cancer.

**H. Breast cancer**

Authorization of 12 months may be granted for treatment of breast cancer.

**I. Renal cell carcinoma**

Authorization of 12 months may be granted for treatment of relapsed or metastatic renal cell carcinoma.

**J. Soft tissue sarcoma**

**Angiosarcoma**

Reference number(s)
1891-A

Authorization of 12 months may be granted for treatment of angiosarcoma, as single agent therapy.

**Solitary fibrous tumor/hemangiopericytoma**

Authorization of 12 months may be granted for treatment of solitary fibrous tumor or hemangiopericytoma, in combination with temozolomide.

**K. Malignant pleural mesothelioma**

Authorization of 12 months may be granted for treatment of malignant pleural mesothelioma, in combination with pemetrexed and either cisplatin or carboplatin, followed by single agent maintenance therapy.

**L. AIDS-related Kaposi sarcoma**

Authorization of 12 months may be granted for treatment of AIDS-related Kaposi sarcoma.

**M. Vulvar cancer**

Authorization of 12 months may be granted for treatment of unresectable locally advanced, recurrent, or metastatic vulvar cancer.

**N. Peritoneal mesothelioma**

Authorization of 12 months may be granted for treatment of peritoneal mesothelioma.

**O. Pericardial mesothelioma**

Authorization of 12 months may be granted for treatment of pericardial mesothelioma.

**P. Tunica vaginalis testis mesothelioma**

Authorization of 12 months may be granted for treatment of tunica vaginalis testis mesothelioma.

**III. CONTINUATION OF THERAPY**

**A. Ophthalmic disorders**

For ophthalmic disorders, authorization of 12 months may be granted for continued treatment of an indication outlined in Section II for members who have demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

**B. All other indications**

For all other indications, authorization of 12 months may be granted for continued treatment of an indication outlined in Section II for members who are experiencing a clinical benefit to therapy or who have not experienced an unacceptable toxicity.

**IV. REFERENCES**

1. Avastin [package insert]. South San Francisco, CA: Genentech, Inc.; June 2019.
2. Mvasi [package insert]. Thousand Oaks, CA: Amgen Inc.; June 2019.
3. Zirabev [package insert]. New York, NY: Pfizer Inc.; June 2019.
4. The NCCN Drugs & Biologics Compendium® © 2020 National Comprehensive Cancer Network, Inc. Available at: <https://www.nccn.org>. Accessed January 7, 2020.
5. Micromedex Solutions [database online]. Truven Health Analytics, Greenwood Village, CO. Available at: <http://www.micromedexsolutions.com>. Accessed January 7, 2020.
6. Chan WM, Lai TY, Lui DT, et al. Intravitreal bevacizumab (Avastin) for myopic choroidal neovascularization: 1-year results of a prospective pilot study. *Br J Ophthalmol*. 2009;93(2):150-154.

Reference number(s)
1891-A

7. Gupta B, Elagouz M, Sivaprasad S. Intravitreal bevacizumab for choroidal neovascularization secondary to causes other than age-related macular degeneration. *Eye*. 2010;24:203-213.
8. CATT Research Group, Martin DF, Maguire MG, et al. Ranibizumab and bevacizumab for neovascular age-related macular degeneration. *N Engl J Med*. 2011;364(20):1897-1908.
9. Russo V, Barone A, Conte E, et al. Bevacizumab compared with macular laser grid photocoagulation for cystoid macular edema in branch retinal vein occlusion. *Retina*. 2009;29:511-5.
10. Michaelides M, Kaines A, Hamilton RD, et al. A prospective randomized trial of intravitreal bevacizumab or laser therapy in the management of diabetic macular edema (BOLT Study) 12-month data: report 2. *Ophthalmology*. 2010;117:1078-1086.
11. Mirshahi A, Rohipoor R, Lashay A, et al. Bevacizumab-augmented retinal laser photocoagulation in proliferative diabetic retinopathy: a randomized double-masked clinical trial. *Eur J Ophthalmol*. 2008;18(2):263-269.
12. Yazdani S, Hendi K, Pakravan M, et al. Intravitreal bevacizumab for neovascular glaucoma: a randomized controlled trial. *J Glaucoma*. 2009;18(8):632-637.
13. Mintz-Hittner HA, Kennedy KA, Chuang AZ, et al. Efficacy of intravitreal bevacizumab for stage 3+ retinopathy of prematurity. *N Engl J Med*. 2011;364(7):603-615.
14. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; 2015. Available at: <https://www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp-2015>.
15. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Diabetic Retinopathy. San Francisco, CA: American Academy of Ophthalmology; 2017. Available at: <https://www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp-updated-2017>.
16. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Retinal Vein Occlusions. San Francisco, CA: American Academy of Ophthalmology; 2015. Available at: <https://www.aao.org/preferred-practice-pattern/retinal-vein-occlusions-ppp-2015>.
17. VanderVeen DK, Melia M, Yang MB, et al. Anti-vascular endothelial growth factor therapy in primary treatment of type 1 retinopathy of prematurity: a report by the American Academy of Ophthalmology. *Ophthalmology*. 2017. May;124(5):619-633.
18. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; [http://online.lexi.com/lco/action/index/dataset/complete\\_ashp](http://online.lexi.com/lco/action/index/dataset/complete_ashp) [available with subscription]. Accessed January 7, 2020.
19. Yong M, Zhou M, Deng G. Photodynamic therapy versus anti-vascular endothelial growth factor agents for polypoidal choroidal vasculopathy: A meta-analysis. *BMC Ophthalmol*. 2015;15:82.
20. Kim JH, Kim JW, Lee TG, Lew YJ. Treatment outcomes in eyes with polypoidal choroidal vasculopathy with poor baseline visual acuity. *J Ocul Pharmacol Ther*. 2015;31(4):241-247.
21. Oishi A. The evidence for the treatment of polypoidal choroidal vasculopathy. *Nippon Ganka Gakkai Zasshi*. 2015;119(11):781-786.
22. Chang YS, Kim JH, Kim KM, et al. Long-term outcomes of anti-vascular endothelial growth factor therapy for polypoidal choroidal vasculopathy. *J Ocul Pharmacol Ther*. 2016;32(4):219-224.
23. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Colon Cancer Version 1.2020. [https://www.nccn.org/professionals/physician\\_gls/pdf/colon.pdf](https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf). Accessed January 7, 2020.
24. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Rectal Cancer Version 1.2020. [https://www.nccn.org/professionals/physician\\_gls/pdf/rectal.pdf](https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf). Accessed January 7, 2020.
25. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Anal Carcinoma Version 1.2020. [https://www.nccn.org/professionals/physician\\_gls/pdf/anal.pdf](https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf). Accessed January 7, 2020.
26. PDQ® Adult Treatment Editorial Board. PDQ Vaginal Cancer Treatment. Bethesda, MD: National Cancer Institute. Updated November 15, 2019. Available at: <https://www.cancer.gov/types/vaginal/hp/vaginal-treatment-pdq>. Accessed January 8, 2020. [PMID: 26389242]

Reference number(s)
1891-A

27. PDQ® Adult Treatment Editorial Board. PDQ Cervical Cancer Treatment. Bethesda, MD: National Cancer Institute. Updated December 12, 2019. Available at: <https://www.cancer.gov/types/cervical/hp/cervical-treatment-pdq>. Accessed January 8, 2020. [PMID: 26389493]