

# Standard Medicare Part B Management

## Avastin and biosimilars -

## Oncology

### Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Avastin	bevacizumab
Alymsys	bevacizumab-maly
Avzivi	bevacizumab-tnjn
Jobevne	bevacizumab-nwgd
Mvasi	bevacizumab-awwb
Vegzelma	bevacizumab-adcd
Zirabev	bevacizumab-bvzr

### 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.

#### FDA-Approved Indications<sup>1-7</sup>

Metastatic Colorectal Cancer (mCRC)

- Avastin/Alymsys/Avzivi/Jobevne/Mvasi/Vegzelma/Zirabev, in combination with intravenous fluorouracil-based chemotherapy, is indicated for the first- or second-line treatment of patients with metastatic colorectal cancer.
- Avastin/Alymsys/Avzivi/Jobevne/Mvasi/Vegzelma/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.

## First-Line Non-Squamous Non-Small Cell Lung Cancer (NSCLC)

Avastin/Alymsys/Avzivi/Jobevne/Mvasi/Vegzelma/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.

## Recurrent Glioblastoma (GBM)

Avastin/Alymsys/Avzivi/Jobevne/Mvasi/Vegzelma/Zirabev is indicated for the treatment of recurrent glioblastoma in adults.

## Metastatic Renal Cell Carcinoma (mRCC)

Avastin/Alymsys/Avzivi/Jobevne/Mvasi/Vegzelma/Zirabev, in combination with interferon alfa, is indicated for the treatment of metastatic renal cell carcinoma.

## Persistent, Recurrent, Or Metastatic Cervical Cancer

Avastin/Alymsys/Avzivi/Jobevne/Mvasi/Vegzelma/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.

## Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

- Avastin/Jobevne/Mvasi/Vegzelma/Zirabev, in combination with carboplatin and paclitaxel, followed by Avastin/Jobevne/Mvasi/Vegzelma/Zirabev 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.
- Avastin/Alymsys/Avzivi/Jobevne/Mvasi/Vegzelma/Zirabev, 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.
- Avastin/Jobevne/Mvasi/Vegzelma/Zirabev, in combination with carboplatin and paclitaxel, or with carboplatin and gemcitabine, followed by Avastin/Jobevne/Mvasi/Vegzelma/Zirabev as a single agent, is indicated for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.

## Hepatocellular Carcinoma

Avastin, in combination with atezolizumab, is indicated for the treatment of patients with unresectable or metastatic hepatocellular carcinoma (HCC) who have not received prior systemic therapy.

## Compendial Uses<sup>8-16</sup>

- Advanced gastric cancer
- Advanced liver carcinoma
- Breast cancer
- Central nervous system (CNS) cancers
  - Circumscribed glioma
  - Diffuse high grade and high grade gliomas
  - Glioblastoma
  - IDH mutant astrocytoma (WHO Grade 2, 3, or 4)
  - Oligodendrolioma (WHO Grade 2 or 3)
  - Intracranial and spinal ependymoma (excludes subependymoma)
  - Medulloblastoma
  - Primary central nervous system lymphoma
  - Meningiomas
  - Limited and extensive brain metastases
  - Metastatic spine tumors
  - Primary spinal cord tumors
- Necrosis of central nervous system due to exposure to ionizing radiation
- Pleural mesothelioma, Peritoneal mesothelioma, Pericardial mesothelioma, Tunica vaginalis testis mesothelioma
- Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer
- Soft tissue sarcoma
  - Angiosarcoma
  - Solitary fibrous tumor/Hemangiopericytoma
- Uterine neoplasms/Endometrial carcinoma
- Vulvar carcinoma
- Vaginal cancer
- Cervical cancer
- Small bowel adenocarcinoma
- Ampullary adenocarcinoma
- Appendiceal adenocarcinoma

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- Anal adenocarcinoma
- Renal cell carcinoma
- Hepatocellular carcinoma

## Nationally Covered Indications<sup>10,11</sup>

CMS covers bevacizumab for use in specific clinical trials (NCI-CMS Pilot Project). Refer to the Appendix for a list of these covered clinical trials.

For non-oncology indications, please see the Avastin/Alymsys/Avzivi/Jobevne/Mvasi/Vegzelma/Zirabev – Ocular & Other MedB policy.

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

## Coverage Criteria

### Colorectal Cancer<sup>1-8,12-14</sup>

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

### Non-Small Cell Lung Cancer<sup>1-8</sup>

Authorization of 12 months may be granted for treatment of symptomatic local, recurrent, unresectable, advanced or metastatic non-squamous non-small cell lung cancer.

### Renal Cell Cancer<sup>1-8</sup>

Authorization of 12 months may be granted for treatment of relapsed or stage IV renal cell cancer.

### Cervical Cancer<sup>1-8</sup>

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

### Vaginal Cancer<sup>8</sup>

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

## Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer<sup>1-8</sup>

Authorization of 12 months may be granted for treatment of epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, and malignant sex cord stromal tumors.

## Hepatocellular Carcinoma<sup>1,8,9</sup>

Authorization of 12 months may be granted for treatment of unresectable, advanced or extrahepatic/metastatic hepatocellular carcinoma.

Authorization of 12 months may be granted for adjuvant treatment of operable hepatocellular carcinoma, when the member is at a high risk of recurrence and the requested medication will be used in combination with atezolizumab.

## Gastric Cancer<sup>9</sup>

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

## Central Nervous System (CNS) Cancer<sup>1-8</sup>

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

- Circumscribed glioma
- Diffuse high grade and high grade gliomas
- Glioblastoma
- IDH mutant astrocytoma (WHO Grade 2, 3, or 4)
- Oligodendrogloma (WHO Grade 2 or 3)
- Intracranial and spinal ependymoma (excluding subependymoma)
- Medulloblastoma
- Primary central nervous system lymphoma
- Meningiomas
- Limited and extensive brain metastases
- Metastatic spine tumors
- Primary spinal cord tumors

## Necrosis of Central Nervous System Due to Exposure to Ionizing Radiation<sup>9</sup>

Authorization of 3 months may be granted for treatment of central nervous system necrosis due to exposure to ionizing radiation.

## **Uterine Neoplasms/Endometrial Carcinoma<sup>8,15</sup>**

Authorization of 12 months may be granted for treatment of progressive, persistent, recurrent, or metastatic uterine neoplasms or endometrial carcinoma.

## **Mesothelioma<sup>8,9</sup>**

Authorization of 12 months may be granted for treatment of pleural mesothelioma, peritoneal mesothelioma, pericardial mesothelioma, or tunica vaginalis testis mesothelioma when any of the following criteria are met:

- As first-line therapy in combination with pemetrexed and either cisplatin or carboplatin, followed by single-agent maintenance bevacizumab
- As subsequent therapy in combination with pemetrexed and either cisplatin or carboplatin if immunotherapy was administered as first-line treatment

Authorization of 12 months may be granted for treatment of peritoneal mesothelioma, pericardial mesothelioma, or tunica vaginalis testis mesothelioma when used in combination with atezolizumab as subsequent therapy.

## **Breast Cancer<sup>9,15</sup>**

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

## **Soft Tissue Sarcoma<sup>8,16</sup>**

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

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

## **Vulvar Carcinoma<sup>8</sup>**

Authorization of 12 months may be granted for treatment of advanced, recurrent, or metastatic vulvar carcinoma, including squamous cell carcinoma and adenocarcinoma.

## **Small Bowel Adenocarcinoma<sup>8</sup>**

Authorization of 12 months may be granted for treatment of small bowel adenocarcinoma.

## **Ampullary Adenocarcinoma<sup>8</sup>**

Authorization of 12 months may be granted for treatment of intestinal-type ampullary adenocarcinoma that is progressive, unresectable, or metastatic.

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## NCD Indications<sup>10,11</sup>

Authorization of 12 months may be granted for treatment of patients enrolled in any of the studies listed in the Appendix section.

## Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 3 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used to treat central nervous system necrosis due to exposure to ionizing radiation.
- The member is receiving benefit from therapy.

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used to treat an indication in the coverage criteria section (excluding central nervous system necrosis due to exposure to ionizing radiation).
- The member is receiving benefit from therapy. Benefit is defined as:
  - No evidence of unacceptable toxicity while on the current regimen and
  - No evidence of disease progression while on the current regimen.

## Appendix

### NCI/CTEP-Sponsored Studies Selected for Inclusion in NCI-CMS Pilot Project (Studies in Various Stages of Development)

Study ID #	Study Title
C80405	Phase III Trial of Irinotecan/5-FU/Leucovorin or Oxaliplatin/5FU/Leucovorin with Bevacizumab, or Cetuximab, or with the combination of Bevacizumab and Cetuximab for Patients with Untreated Metastatic Adenocarcinoma of the Colon or Rectum

Study ID #	Study Title
E2204	An Intergroup Randomized Phase II Study of Bevacizumab or Cetuximab in Combination with Gemcitabine and in Combination with Chemoradiation (Capecitabine and Radiation) in Patients with Completely-Resected Pancreatic Carcinoma
E4203	Phase II Study of Treatment Selection Based Upon Tumor Thymidylate Synthase Expression in Previously Untreated Patients with Metastatic Colorectal Cancer
E5202	Randomized Phase III Study Comparing 5-FU, Leucovorin and Oxaliplatin versus 5-FU, Leucovorin, Oxaliplatin and Bevacizumab in Patients with Stage II Colon Cancer at High Risk for Recurrence to Determine Prospectively the Prognostic Value of Molecular Markers
E5204	Intergroup Randomized Phase III Study of Post-Operative Oxaliplatin, 5-Fluorouracil and Leucovorin with or without Bevacizumab in Patients with Stage II or III Rectal Cancer Receiving Pre-Operative Radiation and a 5-Fluorouracil-Based Regimen
NSABP-R-04	A Clinical Trial Comparing Preoperative Radiation Therapy and Capecitabine with or without Oxaliplatin with Preoperative Radiation Therapy and Continuous Intravenous Infusion 5-Fluorouracil with or without Oxaliplatin in the Treatment of Patients with Operable Carcinoma of the Rectum
RTOG-0522	Phase III Trial of Concurrent Accelerated Radiation & Cisplatin vs Concurrent Accelerated Radiation, Cisplatin, & Cetuximab (Followed by Surgery for Selected Patients) for Stage III & IV Head & Neck Carcinomas
S0502	Phase III Randomized Study of Imatinib, with or without Bevacizumab, in Patients with Metastatic or Unresectable Gastrointestinal Stromal Tumors
7325	Dose-Dense and Dose-Intense Alternating Irinotecan/Capecitabine & Oxaliplatin/Capecitabine: Phase I in Solid Tumors and Phase II with Bevacizumab as First-Line Therapy of Advanced Colorectal Cancer

## Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Avastin, Alymsys, Avzivi, Jobevne, Mvasi, Vegzelma, and Zirabev.
- The available compendium
  - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
  - Micromedex DrugDex

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- American Hospital Formulary Service- Drug Information (AHFS-DI)
- Lexi-Drugs
- Clinical Pharmacology
- NCCN Guideline: Vulvar cancer
- NCCN Guideline: Cervical cancer
- NCCN Guideline: Small bowel adenocarcinoma
- NCCN Guideline: Peritoneal mesothelioma
- NCCN Guideline: Pediatric central nervous system cancers
- NCCN Guideline: Pleural mesothelioma
- NCCN Guideline: Non-small cell lung cancer
- NCCN Guideline: Hepatocellular carcinoma
- NCCN Guideline: Central nervous system cancers
- NCCN Guideline: Ampullary adenocarcinoma
- NCCN Guideline: Ovarian cancer, including fallopian tube cancer and primary peritoneal cancer
- NCCN Guideline: Kidney cancer
- NCCN Guideline: Uterine neoplasms
- NCCN Guideline: Soft tissue sarcoma
- NCCN Guideline: Colon cancer
- NCCN Guideline: Rectal cancer
- NCCN Guideline: Vaginal cancer
- National Coverage Determination (NCD) for Anti-cancer Chemotherapy for Colorectal Cancer (110.17)
- NCI/CTEP-Sponsored Studies Selected for Inclusion in NCI-CMS Pilot Project

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Avastin, Alymsys, Avzivi, Jobevne, Mvasi, Vegzelma, and Zirabev are covered in addition to the following:

- Inclusion in NCI/CTEP-sponsored studies selected for inclusion in NCI-CMS pilot project
- Advanced gastric cancer
- Advanced liver carcinoma
- Breast cancer
- Central nervous system (CNS) cancers
  - Circumscribed glioma
  - Diffuse high grade and high grade gliomas
  - Glioblastoma
  - IDH mutant astrocytoma (WHO Grade 2, 3, or 4)

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- Oligodendrolioma (WHO Grade 2 or 3)
- Intracranial and spinal ependymoma (excludes subependymoma)
- Medulloblastoma
- Primary central nervous system lymphoma
- Meningiomas
- Limited and extensive brain metastases
- Metastatic spine tumors
- Primary spinal cord tumors
- Necrosis of central nervous system due to exposure to ionizing radiation
- Pleural mesothelioma, Peritoneal mesothelioma, Pericardial mesothelioma, Tunica vaginalis testis mesothelioma
- Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer
- Soft tissue sarcoma
  - Angiosarcoma
  - Solitary fibrous tumor/Hemangiopericytoma
- Uterine neoplasms/Endometrial carcinoma
- Vulvar carcinoma
- Vaginal cancer
- Cervical cancer
- Small bowel adenocarcinoma
- Ampullary adenocarcinoma
- Appendiceal adenocarcinoma
- Anal adenocarcinoma
- Renal cell carcinoma
- Hepatocellular carcinoma

## Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using bevacizumab for the below listed indications can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

- Central nervous system (CNS) cancers

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- Circumscribed glioma
- Diffuse high grade and high grade gliomas
- Glioblastoma
- IDH mutant astrocytoma (WHO Grade 2, 3, or 4)
- Oligodendrolioma (WHO Grade 2 or 3)
- Intracranial and spinal ependymoma (excludes subependymoma)
- Medulloblastoma
- Primary central nervous system lymphoma
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- Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer
- Soft tissue sarcoma
  - Angiosarcoma
  - Solitary fibrous tumor/Hemangiopericytoma
- Uterine neoplasms/Endometrial carcinoma
- Vulvar carcinoma
- Vaginal cancer
- Cervical cancer
- Small bowel adenocarcinoma
- Ampullary adenocarcinoma
- Appendiceal adenocarcinoma
- Anal adenocarcinoma
- Renal cell carcinoma
- Hepatocellular carcinoma

Support for using bevacizumab for advanced gastric cancer, advanced liver carcinoma and breast cancer can be found in the Micromedex DrugDex database. Use of information in the DrugDex database for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

Use of bevacizumab in an NCI/CTE-sponsored study is covered according to the conditions outlined in National Coverage Determination Manual section 110.17 Anti-Cancer Chemotherapy for Colorectal Cancer.

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## References

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