Reference number(s)
2477-A

STANDARD MEDICARE PART B MANAGEMENT

AVASTIN (bevacizumab) – Oncology
MVASI (bevacizumab-awwb) – Oncology
ZIRABEV (bevacizumab-bvzr) – Oncology

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)
   i. Avastin/Mvasi/Zirabev, in combination with intravenous fluorouracil-based chemotherapy, is indicated for the first- or second-line treatment of patients with metastatic colorectal cancer.
   ii. Avastin/Mvasi/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 Avastin/Mvasi/Zirabev-containing regimen.
2. First-line non-squamous non-small cell lung cancer (NSCLC)
   Avastin/Mvasi/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 (GBM)
   Avastin/Mvasi/Zirabev is indicated for the treatment of recurrent glioblastoma in adults.
4. Metastatic renal cell carcinoma (mRCC)
   Avastin/Mvasi/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/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
   i. Avastin/Mvasi/Zirabev, in combination with carboplatin and paclitaxel, followed by Avastin/Mvasi/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.
   ii. Avastin/Mvasi/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.
   iii. Avastin/Mvasi/Zirabev, in combination with carboplatin and paclitaxel, or with carboplatin and gemcitabine, followed by Avastin/Mvasi/Zirabev as a single agent, is indicated for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.
7. 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.

B. Compendial Uses
1. Advanced gastric cancer
2. Advanced liver carcinoma
3. Breast cancer for recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-negative disease
4. Central nervous system (CNS) cancers
   i. Low-grade (WHO Grade 1 or 2) glioma
   ii. Intracranial and spinal ependymoma (excludes subependymoma)
   iii. Anaplastic gliomas
   iv. Medulloblastoma
   v. Primary central nervous system lymphoma
   vi. Meningiomas
   vii. Limited and extensive brain metastases
   viii. Metastatic spine tumors
5. Necrosis of central nervous system due to exposure to ionizing radiation
6. Malignant pleural mesothelioma
7. Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer
   i. Carcinosarcoma (malignant mixed Müllerian tumors)
   ii. Clear cell carcinoma
   iii. Mucinous carcinoma
   iv. Malignant sex cord-stromal tumors
   v. Endometrioid carcinoma
   vi. Serous carcinoma
   vii. Ovarian borderline epithelial tumors (low malignant potential) with invasive implants
8. Soft tissue sarcoma
   i. Angiosarcoma
   ii. Solitary fibrous tumor/Hemangiopericytoma
9. Uterine neoplasms/Endometrial carcinoma
10. Vulvar squamous cell carcinoma
11. Small bowel adenocarcinoma, including advanced ampullary cancer
12. Appendiceal carcinoma
13. Anal adenocarcinoma
14. Renal cell carcinoma
15. Peritoneal mesothelioma
16. Pericardial mesothelioma
17. Tunica vaginalis testis mesothelioma

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

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

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II. CRITERIA FOR INITIAL APPROVAL

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

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

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

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

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, primary peritoneal cancer:
1. Epithelial ovarian cancer, including:
    i. Carcinosarcoma (malignant mixed Müllerian tumors)
    ii. Clear cell carcinoma
    iii. Mucinous carcinoma
    iv. Endometrioid carcinoma
    v. 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. Hepatocellular carcinoma
Authorization of 12 months may be granted for treatment of unresectable or metastatic hepatocellular carcinoma, when the requested medication will be used as initial treatment in combination with atezolizumab.

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

H. Liver cancer
Authorization of 12 months may be granted for treatment of liver cancer.

I. Central nervous system (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 (excluding subependymoma)
3. Anaplastic gliomas
4. Low-grade (WHO Grade 1 or 2) glioma
5. Medulloblastoma
6. Primary central nervous system lymphoma
7. Meningiomas
8. Limited and extensive brain metastases
9. Metastatic spine tumors

J. Necrosis of central nervous system due to exposure to ionizing radiation

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

K. Uterine neoplasms/Endometrial carcinoma
Authorization of 12 months may be granted for treatment of progressive, advanced, recurrent, or metastatic uterine neoplasms or endometrial carcinoma.

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

M. Breast cancer
Authorization of 12 months may be granted for treatment of recurrent or metastatic breast cancer.

N. Soft tissue sarcoma
1. Angiosarcoma
   Authorization of 12 months may be granted for treatment of angiosarcoma, as single agent therapy.
2. Solitary fibrous tumor/hemangiopericytoma
   Authorization of 12 months may be granted for treatment of solitary fibrous tumor or hemangiopericytoma, in combination with temozolomide.

O. Vulvar squamous cell carcinoma
Authorization of 12 months may be granted for treatment of unresectable locally advanced, recurrent, or metastatic vulvar squamous cell carcinoma.

P. Small bowel adenocarcinoma
Authorization of 12 months may be granted for treatment of small bowel adenocarcinoma, including advanced ampullary cancer.

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

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

S. Tunica Vaginalis Testis Mesothelioma
Authorization of 12 months may be granted for treatment of tunica vaginalis testis mesothelioma.

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

III. CONTINUATION OF THERAPY

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

A. Authorization for 3 months may be granted when all of the following criteria are met:
   1. The member is currently receiving therapy with Avastin, Mvasi, or Zirabev

2. Avastin, Mvasi, or Zirabev is being used to treat central nervous system necrosis due to exposure to ionizing radiation
3. The member is receiving benefit from therapy.

B. Authorization for 12 months may be granted when all of the following criteria are met:
1. The member is currently receiving therapy with Avastin, Mvasi, or Zirabev
2. Avastin, Mvasi, or Zirabev is being used to treat an indication enumerated in Section II (excluding central nervous system necrosis due to exposure to ionizing radiation)
3. The member is receiving benefit from therapy. Benefit is defined as:
   i. No evidence of unacceptable toxicity while on the current regimen and
   ii. No evidence of disease progression while on the current regimen.

IV. 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/5-FU/Leucovorin with Bevacizumab, or Cetuximab, or with the combination of Bevacizumab and Cetuximab for Patients with Untreated Metastatic Adenocarcinoma of the Colon or Rectum
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

V. REFERENCES

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