Bevacizumab:

Alymsys®; Avastin®; Avzivi®; Jobevne™; Mvasi®; Vegzelma®; Zirabev®

(Intravenous)

ONCOLOGY

-E-

Document Number: OHSU HEALTHSERVICES-0450

Date Reviewed: 08/2025

Date of Origin: 05/01/2019

Dates Approved: 05/2019, 07/2019, 09/2019, 10/2019, 01/2020, 04/2020, 07/2020, 10/2020, 01/2021, 04/2021, 07/2021, 10/2021, 01/2022, 04/2022, 06/2022, 10/2022, 12/2022, 01/2023, 04/2023, 07/2023, 10/2023, 01/2024, 04/2024, 07/2024, 08/2024, 10/2024, 11/2024, 12/2024, 01/06/2025, 04/07/2025, 05/05/2025, 06/05/2025, 06/24/2025, 08/05/2025, 10/02/2025

I. Length of Authorization [9]

- Initial: Prior authorization validity will be provided initially for 6 months, unless otherwise specified.
  - Adult CNS Cancers (symptom management): Prior authorization validity will be provided for twelve (12) weeks.
- Renewal: Prior authorization validity may be renewed every 6 months thereafter, unless otherwise specified.
  - Adult CNS Cancers (symptom management): Prior authorization validity may NOT be renewed.

II. Dosing Limits

1. Max Units (per dose and over time) [HCPCS Unit]:

- Small Bowel Adenocarcinoma & Ampullary Adenocarcinoma: 180 billable units per 42 days
- NSCLC, Cervical Cancer, HCC, Vaginal Cancer, Vulvar Cancer, Endometrial Carcinoma & Mesotheliomas: 170 billable units per 21 days
- CRC & Appendiceal Adenocarcinoma, CNS Cancers, RCC, & All other indications: 360 billable units per 42 days

III. Initial Approval Criteria [1-7]

Prior authorization validity is provided in the following conditions:

Mvasi™ (bevacizumab-awwb) and **Zirabev™** (bevacizumab-bvzr) are the preferred bevacizumab products.

- Patient must have a contraindication, intolerance, or failure of Mvasi™ (bevacizumab-awwb) and Zirabev™ (bevacizumab-bvzr) prior to the consideration of another bevacizumab product.

- Patient is at least 18 years of age, unless otherwise specified; **AND**

Universal Criteria [1-7]

- Patient has no recent history of hemoptysis (i.e., the presence of ≥2.5 mL of blood in sputum); **AND**
- Patient must not have had a surgical procedure within the preceding 28 days or have a surgical wound that has not fully healed; **AND**

Ampullary Adenocarcinoma ‡ [8]

- Used in combination with a fluoropyrimidine- (e.g., 5-fluorouracil/5-FU or capecitabine) based regimen for intestinal type disease; **AND**
  - Used as first-line therapy for metastatic disease; **OR**
  - Used for disease progression

Adult Central Nervous System (CNS) Cancers † ‡ Φ [1-8,10,29,30,78e,87e,94e,148e,150e]

- Used as single-agent for symptomatic mass effect, radiation necrosis, brain edema; **AND**
  - Patient has a diagnosis of one of the following CNS cancers ‡:
    - Circumscribed Glioma
    - Primary CNS Lymphoma
    - Meningiomas
    - Brain or Spine metastases
    - Primary Spinal Cord Tumors
    - Medulloblastoma
    - Glioblastoma/Gliosarcoma
    - H3-mutated high-grade glioma/High-grade astrocytoma with piloid features (HGAP)/Pleomorphic xanthoastrocytoma (PXA) WHO grade 3
    - IDH-mutant Astrocytoma (WHO Grade 2-4)
    - IDH-mutant, 1p19q codeleted Oligodendroglioma (WHO Grade 2 or 3)

  - Intracranial or Spinal Ependymoma *(excluding subependymoma)*; **OR**

- Used for recurrent or progressive disease; **AND**
  - Patient has a diagnosis of one of the following CNS cancers:
    - Glioblastoma/Gliosarcoma/H3-mutated high-grade glioma **† ‡**
    - IDH-mutant Astrocytoma (WHO Grade 3 or 4) **‡**; **AND**
    - Used as a single agent; **OR**
    - Used in combination with carmustine, lomustine, or temozolomide; **AND**
      - Patient has failed bevacizumab monotherapy; **OR**
  - Used in combination with temozolomide and irinotecan for Medulloblastoma *(recurrent disease only)* **‡***;* **OR**
  - Used as a single agent for surgically inaccessible Meningiomas when radiation is not possible **‡**; **OR**
- Used as single agent for Neurofibromatosis type 2 vestibular schwannomas with hearing loss **‡**

Cervical Cancer † ‡ [1-8,32,51,62,66,210e-213e]

- Patient has persistent, recurrent, or metastatic disease; **AND**
  - Patient has adenocarcinoma, adenosquamous, or squamous cell carcinoma; **AND**
    - Used in combination with paclitaxel AND either cisplatin, carboplatin, or topotecan**^**; **AND**
      - Used as first-line therapy; **OR**
    - Used in combination with pembrolizumab, paclitaxel, AND either cisplatin or carboplatin**^**; **AND**
      - Tumor expresses PD-L1 (Combined Positive Score [CPS] ≥1) as determined by an FDA-approved or CLIA compliant testv; **AND**
      - Disease is not amenable to curative treatment (i.e., surgery and/or radiation); **AND**
      - Used as first-line therapy; **OR**
    - Used in combination with atezolizumab, paclitaxel, AND either cisplatin or carboplatin **¤**; **AND**
      - Used as first-line therapy; **OR**
    - Used as a single agent as subsequent therapy; **AND**

      > Patient must demonstrate an inadequate response to a generically available regimen, unless there is a contraindication or intolerance, prior to approval of bevacizumab (e.g., pemetrexed, topotecan, etc. [*see NCCN Cervical Cancer guidelines for complete list of alternative regimens*])

^ Bevacizumab may be continued as a maintenance therapy

¤ Atezolizumab and bevacizumab may be continued as a maintenance therapy

Colorectal Cancer (CRC) ¥ † ‡ [1-8,21-26,49,52]

- Will not be used as part of adjuvant treatment; **AND**
- Will not be used in combination with an anti-EGFR agent (e.g., panitumumab or cetuximab); **AND**
    - Used in combination with a fluoropyrimidine- (e.g., 5-fluorouracil/5-FU or capecitabine) based regimen as first-line or subsequent therapy for metastatic, unresectable (or medically inoperable), or advanced disease; **OR**
    - Used in combination with irinotecan as initial treatment for unresectable metastatic disease; **AND**
        - Patient received previous FOLFOX or CapeOX within the past 12 months; **OR**
    - Used in combination with irinotecan-based therapy as subsequent therapy for advanced or metastatic disease; **OR**
    - Used in combination with trifluridine and tipiracil as subsequent therapy for advanced or metastatic disease; **AND**
        - Patient progressed through all available regimens (e.g., oxaliplatin-based therapy, irinotecan-based therapy, fluoropyrimidine-based therapy, etc.)*; **OR**
    - Used as primary treatment for T3, N Any; T1-2, N1-2; T4, N Any, or locally unresectable (or medically inoperable) rectal cancer; **AND**
        - Used in combination with a fluoropyrimidine- (e.g., 5-fluorouracil/5-FU or capecitabine) based regimen; **AND**
            - Used if resection is contraindicated following total neoadjuvant therapy; **OR**
            - Used if resection is contraindicated following neoadjuvant/definitive immunotherapy

**Refer to NCCN Colon and Rectal Cancer guidelines for regimens.*

¥ Note: NCCN recommends universal MMR or MSI testing in all newly diagnosed patients. If deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) or polymerase epsilon/delta (POLE/POLD1) mutation with ultra-hypermutated phenotype (e.g., TMB>50 mut/Mb), treatment should include checkpoint inhibitor immunotherapy if the patient is a candidate.

Appendiceal Adenocarcinoma – Colon Cancer ¥ ‡ [8,49]

- Used as initial therapy for advanced or metastatic disease; **AND**
    - Used in combination with a fluoropyrimidine- (e.g., 5-fluorouracil/5-FU or capecitabine) based regimen; **OR**
- Used as subsequent therapy for progression of advanced or metastatic disease; **AND**
    - Used in combination with a fluoropyrimidine- (e.g., 5-fluorouracil/5-FU or capecitabine) or irinotecan-based regimen; **OR**

- Used in combination with trifluridine and tipiracil; **AND**
  - Patient progressed through all available regimens (e.g., oxaliplatin-based therapy, irinotecan-based therapy, therapy without irinotecan or oxaliplatin, etc.)*

**Refer to NCCN Colon Cancer guidelines for regimens.*

¥ Note: NCCN recommends universal MMR or MSI testing in all newly diagnosed patients. If deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) or polymerase epsilon/delta (POLE/POLD1) mutation with ultra-hypermutated phenotype (e.g., TMB>50 mut/Mb), treatment should include checkpoint inhibitor immunotherapy if the patient is a candidate.

Endometrial Carcinoma (Uterine Neoplasms) ‡ [8,39,67,130e-133e]

- Used as a single agent as subsequent therapy for recurrent disease that has progressed on prior cytotoxic chemotherapy; **OR**
- Used in combination with carboplatin and paclitaxel, and continued as single agent maintenance therapy; **AND**
  - Used for recurrent disease *(excluding first-line use for isolated metastases)*; **OR**
  - Used as primary or adjuvant therapy (*stage III-IV with measurable disease only*)

Hepatocellular Carcinoma (HCC) † ‡ Φ [1,8,18,19,56,161e,232e]

- Used in combination with atezolizumab; **AND**
- Patient does not have Child-Turcotte-Pugh (CTP) Class C liver disease; **AND**
  - Used as first-line therapy; **AND**
    - Use of bevacizumab will be restricted to patients with a contraindication or intolerance to tremelimumab/durvalumab; **AND**
      - Patient has unresectable disease †; **OR**
      - Patient has extrahepatic/metastatic disease and is deemed ineligible for resection, transplant, or locoregional therapy; **OR**
  - Used as subsequent therapy for progression on or after systemic therapy; **AND**
    - Patient has not received previous treatment with bevacizumab or a checkpoint inhibitor; **AND**
    - Patient received previous treatment with sorafenib or lenvatinib, unless contraindicated

Peritoneal* Mesothelioma (PeM) ‡ [8,46,47,53,179e,183e]

- Used as first-line therapy; **AND**
  - Used in combination with pemetrexed AND either cisplatin or carboplatin; **AND**
    - Patient has one or more of the following:
      - Medically inoperable disease
      - Complete cytoreduction is not achievable

- Presence of any high-risk features**
- Disease has progressed following CRS + HIPEC and no previous adjuvant systemic therapy was given; **OR**

- Used as subsequent therapy; **AND**
  - Used in combination with pemetrexed AND either cisplatin or carboplatin; **AND**
    - Immunotherapy was administered as first-line treatment; **OR**
    - Used as a rechallenge if pemetrexed-based treatment was administered first-line with good response; **OR**
  - Used in combination with atezolizumab; **AND**
    - Patient has not received previous therapy with immune checkpoint inhibitors; **AND**
    - Patient received previous treatment with platinum and pemetrexed, unless contraindicated

**Note: May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma.*

***High-risk features include Ki-67 >9%, nodal metastasis, thrombocytosis, PS=2, high disease burden/incomplete cytoreduction (Peritoneal Cancer Index [PCI] >17), completeness of cytoreduction (cc) score >1, biphasic/sarcomatoid histology, or bicavitary disease.*

Pleural* Mesothelioma (PM) ‡ [8,41,53,134e]

- Used in combination with pemetrexed AND either cisplatin or carboplatin; **AND**
  - Used as first-line therapy; **AND**
    - Patient has unresectable disease not amenable to curative surgery; **OR**
  - Used as subsequent therapy; **AND**
    - Immunotherapy was administered as first-line treatment; **OR**
    - Used as a rechallenge if pemetrexed-based treatment was administered first-line with good response

**Note: May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma.*

Non-Squamous Non-Small Cell Lung Cancer (NSCLC) † ‡ [1-8,14,16,17,27,28,38e-40e,44e,169e]

- Used for recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease with no evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**
  - Used as first-line therapy; **AND**
    - Used in combination with erlotinib for EGFR exon 19 deletion or exon 21 L858R mutations; **OR**
    - Used in combination with carboplatin and paclitaxel †; **OR**
    - Used for one of the following:

- Tumor is negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive)
- Tumor is positive for one of the following molecular biomarkers: EGFR exon 20, BRAF V600E, NTRK1/2/3 gene fusion, MET exon 14 skipping, ERBB2 (HER2), or NRG1 gene fusion; **AND**

➢ Used in combination with one of the following:

♦ Pemetrexed AND either carboplatin or cisplatin in patients with contraindications¥ to PD-1 or PD-L1 inhibitors

♦ Atezolizumab, carboplatin, and paclitaxel; **AND**

In combination with atezolizumab, carboplatin, and paclitaxel ONLY:

- Use of bevacizumab will be restricted to patients with a contraindication or intolerance to cemiplimab/(paclitaxel or pemetrexed)/(carboplatin or cisplatin); **OR**

- Used as subsequent therapy; **AND**
  - Used in combination with atezolizumab, carboplatin, and paclitaxel *(excluding use in patients who have received prior PD-1/PD-L1 inhibitor therapy)*; **AND**
    - Used for one of the following:
      - EGFR S768I, L861Q, and/or G719X mutation positive tumors AND patient received prior targeted therapy§ for those aberrations
      - BRAF V600E mutation, NTRK1/2/3 gene fusion, or MET exon 14 skipping mutation positive tumors; **AND**

➢ Use of bevacizumab will be restricted to patients with a contraindication or intolerance to cemiplimab/(paclitaxel or pemetrexed)/(carboplatin or cisplatin); **OR**

–
  - Patient has contraindications¥ to PD-1 or PD-L1 inhibitors; **AND**
    - Used in combination with one of the following:
      - Carboplatin and paclitaxel
      - Pemetrexed AND either carboplatin or cisplatin; **AND**
    - Used for one of the following:
      - EGFR exon 19 deletion or exon 21 L858R mutation, EGFR S768I, L861Q, and/or G719X mutation, ALK rearrangement, RET rearrangement or ROS1 rearrangement positive tumors AND patient received prior targeted therapy§ for those aberrations
      - BRAF V600E mutation, NTRK1/2/3 gene fusion, or MET exon 14 skipping mutation positive tumors

- PD-L1 expression positive (PD-L1 ≥ 1%) tumors that are negative for actionable molecular biomarkers* after prior PD-1/PD-L1 inhibitor therapy but no prior platinum-containing chemotherapy; **OR**

- Used as continuation maintenance therapy in patients who achieved tumor response or stable disease after first-line systemic therapy; **AND**
  - Used as a single agent (*bevacizumab must have been included in patient's first-line regimen*); **OR**
  - Used in combination with pemetrexed following a first-line bevacizumab/pemetrexed/platinum chemotherapy regimen; **OR**
  - Used in combination with atezolizumab following a first-line atezolizumab/carboplatin/paclitaxel/bevacizumab regimen; **OR**
- Used as continuation of therapy following disease progression on erlotinib with bevacizumab; **AND**
  - Patient has asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited progression; **AND**
  - Patient has T790M negative disease

**Note: Actionable molecular genomic biomarkers include EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, NRG1, and ERBB2 (HER2). Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, NRG1 and ERBB2 (HER2), via biopsy and/or plasma testing. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes.*
***¥** Note: Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R; ALK, RET, or ROS1 rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.*
***§** Note: Genomic Aberration/Mutational Driver Targeted Therapies: Refer to guidelines for appropriate use*

Ovarian, Fallopian Tube, and Primary Peritoneal Cancer † ‡ Φ [1-8,15,33-36,54,100e,107e,113e,117e,163e]

- Patient has malignant stage II-IV sex cord-stromal tumors ‡; **AND**
  - Used as a single agent for clinically relapsed disease; **AND**

○ Patient must demonstrate an inadequate response to paclitaxel, unless there is a contraindication or intolerance, prior to approval of bevacizumab; **OR**

- Patient has epithelial* ovarian, fallopian tube, or primary peritoneal cancer †; **AND**
  - Patient has platinum-resistant recurrent low grade serous carcinoma; **AND**
    - Used in combination with oral cyclophosphamide and pembrolizumab; **AND**

- Patient must demonstrate an inadequate response to one of the following, unless there is a contraindication or intolerance, prior to approval of bevacizumab:
  - Bevacizumab ± paclitaxel, oral cyclophosphamide, liposomal doxorubicin, or topotecan
  - Generically available agent or regimen (e.g., liposomal doxorubicin, paclitaxel, etc. [*see NCCN Ovarian Cancer guidelines for complete list of alternatives*]); **OR**

–

- Used in combination with one of the following: oral cyclophosphamide, liposomal doxorubicin, paclitaxel, topotecan, or mirvetuximab soravtansine (in folate receptor-alpha expressing tumors [≥25% positive tumor cells]); **OR**

- Patient has persistent or recurrent disease; **AND**
  - Patient is not experiencing an immediate biochemical relapse (i.e., rising CA-125 without radiographic evidence of disease); **AND**
    - Patient has platinum-sensitive disease; **AND**
      - Used as a single agent; **OR**
      - Used in combination with carboplatin AND either gemcitabine, paclitaxel †, or liposomal doxorubicin; **OR**
    - Patient has platinum-resistant disease; **AND**
      - Used as a single agent; **AND**
        - Patient must demonstrate an inadequate response to a generically available regimen, unless there is a contraindication or intolerance, prior to approval of bevacizumab (e.g., topotecan, etc. [*see NCCN Ovarian Cancer guidelines for complete list of alternative regimens*]); **OR**
      - Used in combination with one of the following: oral cyclophosphamide, gemcitabine, liposomal doxorubicin, paclitaxel, or topotecan; **OR**
      - Used in combination with oral cyclophosphamide and pembrolizumab; **AND**
        - Patient must demonstrate an inadequate response to one of the following, unless there is a contraindication or intolerance, prior to approval of bevacizumab:
          - Bevacizumab ± paclitaxel, liposomal doxorubicin, or topotecan

- Generically available agent or regimen (e.g., liposomal doxorubicin, paclitaxel, etc. [*see NCCN Ovarian Cancer guidelines for complete list of alternatives*]); **OR**

  - Used in combination with mirvetuximab soravtansine (in folate receptor-alpha expressing tumors [25% positive tumor cells]); **OR**

- Used in combination with paclitaxel and carboplatin for rising CA-125 levels or clinical relapse in patients who have received no prior chemotherapy *(mucinous, clear cell, carcinosarcoma, endometrioid, and high-grade serous histology only)*; **OR**
- Used in combination with paclitaxel and carboplatin for recurrence in patients who have received no prior chemotherapy *(low-grade serous carcinoma only)*; **OR**
- Used as maintenance therapy; **AND**
  - Used following primary therapy including bevacizumab; **AND**
    - Used for stage II-IV disease as a single agent in patients that are BRCA1/2 wild-type or unknown *(grade 2/3 endometrioid and high-grade serous histology only)*; **OR**
    - Used for stage III-IV disease in combination with olaparib or niraparib (if unable to tolerate olaparib); **AND**
      - Patient is BRCA1/2 wild-type or unknown AND HR deficient *(grade 2/3 endometrioid and high-grade serous histology only)*; **OR**
      - Patient has a germline or somatic BRCA1/2 mutation *(grade 2/3 endometrioid, high-grade serous, clear cell, carcinosarcoma histology only)*; **OR**
  - Used as a single agent following recurrence therapy with chemotherapy plus bevacizumab for platinum-sensitive disease; **OR**
  - Used as continued treatment for stable disease following neoadjuvant therapy *(endometrioid and serous histology only)*; **AND**
    - Used in combination with carboplatin AND paclitaxel or docetaxel; **OR**
    - Used in combination with oxaliplatin and docetaxel; **OR**
- Used as neoadjuvant therapy *(does not apply to low malignant potential or other non-invasive cancers such as ovarian borderline epithelial tumors)*; **AND**
  - Used in combination with one of the following:
    - Carboplatin AND paclitaxel or docetaxel
    - Oxaliplatin and docetaxel *(excludes use in grade 1 endometrioid carcinoma and low grade serous carcinoma);* **AND**
  - Patient is a poor surgical candidate or has a low likelihood of optimal cytoreduction; **OR**
- Used as adjuvant therapy; **AND**

- Used in combination with oxaliplatin and docetaxel; **AND**
  - Patient has pathologic stage II-IV disease *(excludes use in grade 1 endometrioid carcinoma and low grade serous carcinoma)*; **OR**
  - Used following interval debulking surgery (IDS) in patients with a response or stable disease to neoadjuvant therapy *(endometrioid and serous histology only)*; **AND**
    - Patient is a poor surgical candidate or has a low likelihood of optimal cytoreduction; **OR**
- Used in combination with carboplatin AND paclitaxel or docetaxel; **AND**
  - Patient has pathologic stage III-IV disease; **OR**
  - Used following interval debulking surgery (IDS) in patients with a response or stable disease to neoadjuvant therapy *(endometrioid and serous histology only)*; **AND**
    - Patient is a poor surgical candidate or has a low likelihood of optimal cytoreduction

**Epithelial subtypes include serous, endometrioid, carcinosarcoma (malignant mixed Müllerian tumors [MMMTs] of the ovary), clear cell, mucinous, and borderline epithelial tumors (also known as low malignant potential [LMP] tumors).*

Pediatric Central Nervous System (CNS) Cancers ‡ [8,48,57-61,65,70-76]

- Patient has recurrent or progressive disease; **AND**
  - Patient has medulloblastoma; **AND**
    - Patient is ≥ 3 years of age and ≤ 21 years of age; **AND**
      - Used as part of the TEMR regimen (temozolomide, irinotecan, bevacizumab); **OR**
      - Used as part of MEMMAT regimen (thalidomide, celecoxib, fenofibrate, etoposide, cyclophosphamide, bevacizumab; **OR**
  - Patient has optic pathway glioma; **AND**
    - Patient is < 18 years of age; **AND**
    - Used as subsequent treatment following chemotherapy and/or radiation; **AND**
    - Used as a single agent or in combination with standard therapies (e.g., irinotecan, carboplatin, vinblastine, etc.); **OR**
  - Patient has neurofibromatosis type 2 (NF2) vestibular schwannomas; **AND**
    - Patient is ≥ 6 years of age; **AND**
    - Patient has hearing loss in at least 1 ear; **OR**
- Used as continuation of therapy following disease progression on bevacizumab; **AND**

- Used to preserve vision in patients with optic pathway glioma; **OR**
- Used to preserve hearing in patients with NF2 vestibular schwannomas

Renal Cell Carcinoma (RCC) † ‡ [1-8,31,62e,65e,71e-75e]

- Used in combination with interferon alfa for metastatic disease †; **OR**
- Patient has relapsed or stage IV disease with non-clear cell histology ‡; **AND**
  - Used in combination with everolimus* as first-line therapy; **OR**
  - Used in combination with erlotinib for advanced papillary disease including hereditary leiomyomatosis and renal cell carcinoma (HLRCC)-associated RCC

– ***When used as first-line therapy for stage IV disease, disease must be M1 or unresectable T4, M0***

Small Bowel Adenocarcinoma ‡ [8,20,155e]

- Patient has advanced or metastatic disease; **AND**
- Used in combination with a fluoropyrimidine- (e.g., 5-fluorouracil/5-FU or capecitabine) based regimen; **AND**
  - Used as initial therapy if pMMR/MSS disease; **OR**
  - Used as subsequent therapy if not previously given

Soft Tissue Sarcoma (STS) ‡ [8,38,43]

- Used as a single agent for angiosarcoma; **AND**
- Patient has unresectable disease

Vaginal Cancer ‡ [8,32,62,210e-213e]

- Patient has recurrent or metastatic disease; **AND**
  - Used in combination with paclitaxel AND either cisplatin, carboplatin, or topotecan; **AND**
    - Used as first-line therapy; **OR**
  - Used in combination with pembrolizumab, paclitaxel, AND either cisplatin or carboplatin; **AND**
    - Tumor expresses PD-L1 (CPS ≥1) as determined by an FDA-approved or CLIA compliant testv; **AND**
    - Disease is not amenable to curative treatment (i.e., surgery and/or radiation); **AND**
    - Used as first-line therapy; **OR**
  - Used as a single agent as subsequent therapy; **AND**

    - Patient must demonstrate an inadequate response to a generically available regimen, unless there is a contraindication or intolerance, prior to approval of bevacizumab (e.g., pemetrexed, topotecan, etc. [*see NCCN Vaginal Cancer guidelines for complete list of alternative regimens*])

Vulvar Cancer ‡ [8,32,62]

- Patient has advanced, recurrent, or metastatic disease; **AND**
- Used as first-line therapy; **AND**
  - Used in combination with paclitaxel AND either cisplatin or carboplatin**^**; **OR**
  - Used in combination with pembrolizumab, paclitaxel, AND either cisplatin or carboplatin**∞**; **AND**
    - Disease is not amenable to curative treatment (i.e., surgery and/or radiation)

^ *Bevacizumab may be continued as a maintenance therapy*

∞ *Pembrolizumab and bevacizumab may be continued as a maintenance therapy*

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

Enhanced Oncology Value (EOV) Program – Redacted indications
Uses not listed above have inadequate data to support efficacy and are excluded from prior authorization validity. Other treatment options including, but are not limited to, the following may be appropriate: radiation therapy, surgery, traditional chemotherapy (e.g., platinum, taxane), compassionate use/expanded access programs, clinical trials, supportive care, integrative and complementary therapies.

v *If confirmed using an FDA-approved assay – http://www.fda.gov/companiondiagnostics*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); **Φ** Orphan Drug

IV. Renewal Criteria [1-8,10]

Prior authorization validity may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Duration of authorization has not been exceeded (refer to Section I); **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread, unless otherwise specified; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: gastrointestinal perforations and fistulae, surgical/wound healing complications, hemorrhage,

necrotizing fasciitis, arterial and venous thromboembolic events (ATE & VTE), uncontrolled hypertension, posterior reversible encephalopathy syndrome (PRES), nephrotic syndrome, proteinuria, severe infusion-related reactions, ovarian failure, congestive heart failure (CHF), etc.

V. Dosage/Administration [1-7,9-10,15,20,32,38,39,41-50,55-62,64-66,68-69,72,75]

Indication	Dose
CRC & Appendiceal Adenocarcinoma	Administer 5 to 10 mg/kg intravenously every 2 weeks **OR** 7.5 mg/kg intravenously every 3 weeks until disease progression or unacceptable toxicity.
Small Bowel Adenocarcinoma & Ampullary Adenocarcinoma	Administer 5 mg/kg intravenously every 2 weeks **OR** 7.5 mg/kg intravenously every 3 weeks until disease progression or unacceptable toxicity.
NSCLC, Cervical Cancer, HCC, Vulvar Cancer, Vaginal Cancer, Endometrial Carcinoma & Mesotheliomas (peritoneal, pleural, pericardial, and tunica vaginalis testis)	Administer 15 mg/kg intravenously every 3 weeks until disease progression or unacceptable toxicity.
Adult CNS Cancers	For symptomatic mass effect, radiation necrosis, brain edema: Administer 5 to 10 mg/kg intravenously every 2 weeks up to 12 weeks duration **OR** 7.5 mg/kg intravenously every 3 weeks up to 12 weeks. For Neurofibromatosis type 2 vestibular schwannomas: Administer 7.5 mg/kg intravenously every 3 weeks until disease progression or unacceptable toxicity. For recurrent or progressive disease: Single agent: - Administer 10 mg/kg intravenously every 2 weeks **OR** 5 to 15 mg/kg every 3 weeks until disease progression or unacceptable toxicity. In combination with carmustine, lomustine, or temozolomide; OR temozolomide and irinotecan: - Administer 5 to 10 mg/kg intravenously every 2 weeks
Pediatric CNS Cancers	Optic Pathway Glioma: Administer 10 mg/kg intravenously every 2 weeks. Neurofibromatosis type 2 vestibular schwannomas: Administer 7.5 mg/kg intravenously every 3 weeks. All other indications:

	Administer 10 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity.
RCC	Administer 10 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity.
All Other Indications	Administer 5 to 10 mg/kg intravenously every 2 weeks **OR** 7.5 to 15 mg/kg intravenously every 3 weeks until disease progression or unacceptable toxicity.

VI. Billing Code/Availability Information

HCPCS Code(s):

- J9035 – Injection, bevacizumab, 10 mg; 1 billable unit = 10 mg
- Q5107 – Injection, bevacizumab-awwb, biosimilar, (mvasi), 10 mg; 1 billable unit = 10 mg
- Q5118 – Injection, bevacizumab-bvzr, biosimilar, (zirabev), 10 mg; 1 billable unit = 10 mg
- Q5126 – Injection, bevacizumab-maly, biosimilar, (alymsys), 10 mg; 1 billable unit = 10 mg
- Q5129 – Injection, bevacizumab-adcd, biosimilar, (vegzelma), 10 mg; 1 billable unit = 10 mg
- Q5160 – Injection, bevacizumab-nwgd (jobevne), biosimilar, 10 mg; 1 billable unit = 10 mg *(Effective 01/01/2026)*
- J9999 – Not otherwise classified, antineoplastic drugs *(Avzivi and Jobevne only) (Discontinue use on 01/01/2026 for Jobevne only)*

NDC(s):

- Avastin single-dose vial, 100 mg/4 mL solution for injection: 50242-0060-xx
- Avastin single-dose vial, 400 mg/16 mL solution for injection: 50242-0061-xx
- Mvasi single-dose vial, 100 mg/4 mL solution for injection: 55513-0206-xx
- Mvasi single-dose vial, 400 mg/16 mL solution for injection: 55513-0207-xx
- Zirabev single-dose vial, 100 mg/4 mL solution for injection: 00069-0315-xx
- Zirabev single-dose vial, 400 mg/16 mL solution for injection: 00069-0342-xx
- Alymsys single-dose vial, 100 mg/4 mL solution for injection: 70121-1754-xx
- Alymsys single-dose vial, 400 mg/16 mL solution for injection: 70121-1755-xx
- Vegzelma single-dose vial, 100 mg/4 mL solution for injection: 72606-0011-xx
- Vegzelma single-dose vial, 400 mg/16 mL solution for injection: 72606-0012-xx
- Avzivi single-dose vial, 100 mg/4 mL solution for injection: 82143-0001-xx
- Avzivi single-dose vial, 400 mg/16 mL solution for injection: 82143-0002-xx
- Jobevne single-dose vial, 100 mg/4 mL solution for injection: 83257-0009-xx
- Jobevne single-dose vial, 400 mg/16 mL solution for injection: 83257-0010-xx

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Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD)

Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	No: PA not a priority
Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C17.0	Malignant neoplasm duodenum
C17.1	Malignant neoplasm jejunum
C17.2	Malignant neoplasm ileum
C17.3	Meckel's diverticulum, malignant
C17.8	Malignant neoplasm of overlapping sites of small intestines
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of large intestines
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C22.0	Liver cell carcinoma
C22.3	Angiosarcoma of the liver
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C24.1	Malignant neoplasm of ampulla of Vater
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus

ICD-10	ICD-10 Description
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C45.0	Mesothelioma of pleura
C45.1	Mesothelioma of peritoneum
C45.2	Mesothelioma of pericardium
C45.7	Mesothelioma of other sites
C45.9	Mesothelioma, unspecified
C48.0	Malignant neoplasm of retroperitoneum
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C49.0	Malignant neoplasm of connective and soft tissue of head, face and neck
C49.10	Malignant neoplasm of connective and soft tissue of unspecified upper limb, including shoulder
C49.11	Malignant neoplasm of connective and soft tissue of right upper limb including shoulder
C49.12	Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.20	Malignant neoplasm of connective and soft tissue of unspecified lower limb, including hip
C49.21	Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22	Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C49.3	Malignant neoplasm of connective and soft tissue of thorax
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis

ICD-10	ICD-10 Description
C49.6	Malignant neoplasm of connective and soft tissue of trunk, unspecified
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C51.0	Malignant neoplasm of labium majus
C51.1	Malignant neoplasm of labium minus
C51.2	Malignant neoplasm of clitoris
C51.8	Malignant neoplasm of overlapping sites of vulva
C51.9	Malignant neoplasm of vulva, unspecified
C52	Malignant neoplasm of vagina
C53.0	Malignant neoplasm of endocervix
C53.1	Malignant neoplasm of exocervix
C53.8	Malignant neoplasm of overlapping sites of cervix uteri
C53.9	Malignant neoplasm of cervix uteri, unspecified
C54.0	Malignant neoplasm of isthmus uteri
C54.1	Malignant neoplasm of endometrium
C54.2	Malignant neoplasm of myometrium
C54.3	Malignant neoplasm of fundus uteri
C54.8	Malignant neoplasm of overlapping sites of corpus uteri
C54.9	Malignant neoplasm of corpus uteri, unspecified
C55	Malignant neoplasm of uterus, part unspecified
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.3	Malignant neoplasm of bilateral ovaries
C56.9	Malignant neoplasm of unspecified ovary
C57.00	Malignant neoplasm of unspecified fallopian tube
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C57.10	Malignant neoplasm of unspecified broad ligament
C57.11	Malignant neoplasm of right broad ligament
C57.12	Malignant neoplasm of left broad ligament
C57.20	Malignant neoplasm of unspecified round ligament
C57.21	Malignant neoplasm of right round ligament
C57.22	Malignant neoplasm of left round ligament
C57.3	Malignant neoplasm of parametrium

ICD-10	ICD-10 Description
C57.4	Malignant neoplasm of uterine adnexa, unspecified
C57.7	Malignant neoplasm of other specified female genital organs
C57.8	Malignant neoplasm of overlapping sites of female genital organs
C57.9	Malignant neoplasm of female genital organ, unspecified
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
C70.0	Malignant neoplasm of cerebral meninges
C70.1	Malignant neoplasm of spinal meninges
C70.9	Malignant neoplasm of meninges, unspecified
C71.6	Malignant neoplasm of cerebellum
C71.7	Malignant neoplasm of brain stem
C71.8	Malignant neoplasm of overlapping sites of brain
C71.9	Malignant neoplasm of brain, unspecified
C72.30	Malignant neoplasm of unspecified optic nerve
C72.31	Malignant neoplasm of right optic nerve
C72.32	Malignant neoplasm of left optic nerve
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C79.31	Secondary malignant neoplasm of brain
C83.30	Diffuse large B-cell lymphoma unspecified site
C83.390	Primary central nervous system lymphoma
C83.398	Diffuse large B-cell lymphoma of other extranodal and solid organ sites
C83.59	Lymphoblastic (diffuse) lymphoma, extranodal and solid organ sites
C83.79	Burkitt lymphoma, extranodal and solid organ sites
C83.80	Other non-follicular lymphoma unspecified site
C83.89	Other non-follicular lymphoma extranodal and solid organ sites
C84.49	Peripheral T-cell lymphoma, not elsewhere classified, extranodal and solid organ sites

ICD-10	ICD-10 Description
C85.89	Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C85.99	Non-Hodgkin lymphoma, unspecified, extranodal and solid organ sites
D32.0	Benign neoplasm of cerebral meninges
D32.1	Benign neoplasm of spinal meninges
D32.9	Benign neoplasm of meninges, unspecified
D42.0	Neoplasm of uncertain behavior of cerebral meninges
D42.1	Neoplasm of uncertain behavior of spinal meninges
D42.9	Neoplasm of uncertain behavior of meninges, unspecified
D43.0	Neoplasm of uncertain behavior of brain, supratentorial
D43.1	Neoplasm of uncertain behavior of brain, infratentorial
D43.2	Neoplasm of uncertain behavior of brain, unspecified
D43.4	Neoplasm of uncertain behavior of spinal cord
D43.9	Neoplasm of uncertain behavior of central nervous system, unspecified
G93.6	Cerebral edema
I67.89	Other cerebrovascular disease
I67.9	Cerebrovascular disease, unspecified
Q85.02	Neurofibromatosis, type 2
Q85.03	Schwannomatosis
Q85.83	Von Hippel-Lindau syndrome
Y84.2	Radiological procedure and radiotherapy as the cause of abnormal reaction of the patient, or of later complication, without mention of misadventure at the time of the procedure
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.09	Personal history of malignant neoplasm of other digestive organs
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.42	Personal history of malignant neoplasm of other parts of uterus
Z85.43	Personal history of malignant neoplasm of ovary
Z85.831	Personal history of malignant neoplasm of soft tissue

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under

Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes		
Jurisdiction	**NCD/LCA/LCD Document (s)**	**Contractor**
6, K	A52370	National Government Services, Inc

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC