Bevacizumab:
Avastin®; Mvasi®; Zirabev™; Alymsys®; Vegzelma®
(Intravenous) *ONCOLOGY*

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I. Length of Authorization [8]

Coverage will be provided for 6 months and may be renewed (unless otherwise specified).

- Adult CNS Cancers (symptom management): Coverage will be provided for twelve (12) weeks and may NOT be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

Avastin, Mvasi, Zirabev, Alymsys, Vegzelma:
- 100 mg/4 mL single-dose vial: 3 vials 21 days
- 400 mg/16 mL single-dose vial: 4 vials per 21 days

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

Oncology indications (J9035/Q5107/Q5118/Q5126/Q5129):
- Small Bowel Adenocarcinoma/Ampullary Adenocarcinoma:
  - 60 billable units per 14 days
- NSCLC, Cervical Cancer, HCC, Vulvar Cancer, MPM, & MPeM:
  - 170 billable units per 21 days
- All other indications:
  - 120 billable units per 14 days

III. Initial Approval Criteria [1-5]

Coverage is provided in the following conditions:

- Patient must try and have an inadequate response, contraindication, or intolerance to Mvasi AND Zirabev; **OR**
- Patient is continuing treatment with a different bevacizumab product

Step therapy does not apply to MN residents with metastatic cancer per statute 62Q.1841. https://www.revisor.mn.gov/statutes/cite/62Q.1841

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

Universal Criteria [1-5]

- 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 ‡ [6]

- 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 unresectable localized or metastatic disease; **OR**
  - Used as subsequent therapy for disease progression; **AND**
    - Patient has poor performance status (ECOG PS 2); **OR**
    - Patient has good performance status (ECOG 0-1, with good biliary drainage and adequate nutritional intake) and received prior oxaliplatin-based therapy

Adult Central Nervous System (CNS) Cancers † ‡ Φ [1-6,8,27,28]

- Used as single-agent short-course therapy for symptom management related to radiation necrosis, poorly controlled vasogenic edema, or mass effect; **AND**
  - Patient has a diagnosis of one of the following CNS cancers ‡:
    - Circumscribed Glioma
    - Primary CNS Lymphoma
    - Meningiomas
    - Brain or Spine metastases
    - Medulloblastoma
    - Glioblastoma/Gliosarcoma/H3-mutated high grade glioma
    - 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:
    - IDH-mutant, 1p19q codeleted Oligodendroglioma (WHO Grade 3) ‡ Φ

- 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 as a single agent for Intracranial or Spinal Ependymoma *(excluding subependymoma)* after prior radiation therapy ‡; **OR**
- Used as a single agent for surgically inaccessible Meningiomas when radiation is not possible ‡

Cervical Cancer † ‡ [1-6,30,49]

- Patient has persistent, recurrent, or metastatic disease; **AND**
  - Disease has adenocarcinoma, adenosquamous, or squamous cell carcinoma histology; **AND**
    - Used in combination with paclitaxel AND either cisplatin, carboplatin, or topotecan; **OR**
    - Used in combination with pembrolizumab, paclitaxel, AND cisplatin or carboplatin; **AND**
      - Tumor expresses PD-L1 (Combined Positive Score [CPS] ≥1) as determined by an FDA-approved or CLIA compliant test❖; **OR**
    - Used as a single agent as subsequent therapy; **OR**
  - Patient has small cell neuroendocrine carcinoma of the cervix (NECC); **AND**
    - Used in combination with paclitaxel and topotecan; **OR**
    - Used as a single agent as subsequent therapy

Colorectal Cancer (CRC) † ‡ [1-6,19-24,50]

- Will not be used as part of adjuvant treatment; **AND**
  - Used in combination with a fluoropyrimidine- (e.g., 5-fluorouracil/5-FU or capecitabine) or irinotecan-based regimen as first-line or subsequent therapy for metastatic, unresectable (or medically inoperable), or advanced disease; **AND**
    - Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease; **OR**
    - Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease AND is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **OR**
  - Used in combination with a fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based regimen (not used first line) as second-line therapy for metastatic disease that has progressed on a first-line bevacizumab-containing regimen †; **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.)*; **AND**
    - Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease**; **OR**
    - Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease** AND is not a candidate for or has progressed on checkpoint inhibitor immunotherapy**

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

***Note: Only applies to advanced disease.*

Appendiceal Adenocarcinoma – Colon Cancer ‡ [6,47]

- 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; **AND**
    - Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease; **OR**
    - Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease AND is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **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 following previous oxaliplatin- irinotecan- and/or fluoropyrimidine-based therapy; **AND**
    - Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease; **OR**
    - Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease AND is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **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, therapy without irinotecan or oxaliplatin, etc.)*; **AND**
      - Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease; **OR**
      - Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease AND is not a candidate for or has progressed on checkpoint inhibitor immunotherapy

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

Endometrial Carcinoma (Uterine Neoplasms) ‡ [6,37]

- Used as a single agent for recurrent disease that has progressed on prior cytotoxic chemotherapy; **OR**
- Used in combination with carboplatin and paclitaxel for recurrent disease

Hepatocellular Carcinoma (HCC) † ‡ Φ [1,6,16,17]

- Used as first-line therapy in combination with atezolizumab; **AND**
- Patient has Child-Pugh Class A or B hepatic impairment; **AND**
  - Patient has unresectable* or metastatic disease; **OR**
  - Patient has liver-confined disease that is inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic disease; **OR**
  - Patient has extensive liver tumor burden

**Patients with unresectable Child-Pugh Class B hepatic impairment must not be a transplant candidate.*

Malignant Peritoneal* Mesothelioma (MPeM) ‡ [6,44,51]

- Used as first-line therapy; **AND**
  - Used in combination with pemetrexed AND either cisplatin or carboplatin (if cisplatin ineligible) for unresectable diffuse or recurrent disease; **OR**
- Used as subsequent therapy; **AND**
  - Used in combination with pemetrexed AND either cisplatin or carboplatin (if cisplatin ineligible); **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 (e.g., nivolumab, pembrolizumab, durvalumab, avelumab, cemiplimab, dostarlimab, nivolumab/relatlimab-rmbw, etc.)

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

Malignant Pleural* Mesothelioma (MPM) ‡ [6,39,51]

- Used as first-line therapy; **AND**
  - Used in combination with pemetrexed AND either cisplatin or carboplatin (if cisplatin ineligible); **OR**
- Used as subsequent therapy; **AND**
  - Used in combination with pemetrexed AND either cisplatin or carboplatin (if cisplatin ineligible); **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) † ‡ [1-6,12,14,15,25,26]

- 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 for one of the following:
      - Patients with a performance status (PS) 0-1 who have tumors that are negative for actionable molecular biomarkers* and PD-L1 expression < 1%
      - PD-L1 expression positive (PD-L1 ≥ 1%) tumors that are negative for actionable molecular biomarkers*
      - Patients with a PS 0-1 who are positive for one of the following molecular biomarkers: EGFR exon 20, KRAS G12C, BRAF V600E, NTRK1/2/3 gene fusion, MET exon 14 skipping, RET rearrangement, or ERBB2 (HER2); **AND**
        - Used in combination with one of the following:
          - Carboplatin and paclitaxel †
          - Pemetrexed and either carboplatin or cisplatin in patients with contraindications¥ to PD-1 or PD-L1 inhibitors
          - Atezolizumab, carboplatin, and paclitaxel; **OR**
  - Used as subsequent therapy in patients with a PS 0-1; **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, or ROS1 rearrangement positive tumors AND patient received prior targeted therapy§ for those aberrations
      - BRAF V600E mutation, NTRK1/2/3 gene fusion, MET exon 14 skipping mutation, or RET rearrangement 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; **AND**
    - Used in combination with one of the following:

- Carboplatin and paclitaxel in patients with contraindications¥ to PD-1 or PD-L1 inhibitors
- Pemetrexed and either carboplatin or cisplatin in patients with contraindications¥ to PD-1 or PD-L1 inhibitors
- Atezolizumab, carboplatin, and paclitaxel *(excluding use in patients who have received prior PD-1/PD-L1 inhibitor therapy)*; **OR**

- Used as continuation maintenance therapy in patients who achieved a tumor response or stable disease after first-line systemic therapy; **AND**
  - Used as a single agent *(bevacizumab must have been included in the 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, and ERBB2 (HER2). If there is insufficient tissue to allow testing for all of EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2), repeat biopsy and/or plasma testing should be done. If these are not feasible, 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 rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.*

Ovarian, Fallopian Tube, and Primary Peritoneal Cancer † ‡ Φ [1-6,13,31-34,52]

- Patient has malignant stage II-IV sex cord-stromal tumors ‡; **AND**
  - Used as a single agent for clinically relapsed disease; **OR**
- Patient has epithelial* ovarian, fallopian tube, or primary peritoneal cancer †; **AND**
  - Patient has persistent or recurrent disease; **AND**
    - Bevacizumab has not been used previously; **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; **OR**
  - Used in combination with one of the following: oral cyclophosphamide, gemcitabine, liposomal doxorubicin, paclitaxel, or topotecan †; **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 serous histology only)*; **OR**
- Used as maintenance therapy; **AND**
  - Used for stage II-IV disease following primary therapy including bevacizumab; **AND**
    - Used as a single agent in patients that are BRCA1/2 wild-type or unknown AND homologous recombination (HR) proficient, HR deficient, or status unknown *(grade 2/3 endometrioid and high-grade serous histology only)*; **OR**
    - Used in combination with 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 *(endometrioid and serous histology only)*; **AND**
  - Used in combination with one of the following:
    - Carboplatin AND paclitaxel or docetaxel
    - Oxaliplatin and docetaxel; **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 IB or IC disease *(clear cell, carcinosarcoma, grade 2/3 endometrioid, and high-grade serous histology only)*; **OR**

- Patient has pathologic stage II-IV disease *(mucinous, clear cell, carcinosarcoma, grade 2/3 endometrioid, and high-grade serous histology only)*; **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 II-IV disease *(mucinous, clear cell, carcinosarcoma, borderline epithelial, endometrioid, and serous histology only)*; **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 ‡ [2,47]

- Patient is ≤ 18 years of age; **AND**
- Patient has diffuse high-grade glioma *(excluding oligodendroglioma, IDH-mutant and 1p/19q co-deleted or astrocytoma IDH-mutant)*; **AND**
- Used for palliation of recurrent or progressive disease

Renal Cell Carcinoma (RCC) † ‡ Φ [1-6,29]

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

Small Bowel Adenocarcinoma ‡ [6,18]

- Patient has advanced or metastatic disease; **AND**
- Used in combination with a fluoropyrimidine- (e.g., 5-fluorouracil/5-FU or capecitabine) based regimen

Soft Tissue Sarcoma ‡ [6]

- Used as a single agent for angiosarcoma; **OR**
- Used in combination with temozolomide for solitary fibrous tumor

Vulvar Cancer ‡ [6]

- Used in combination with paclitaxel and cisplatin; **AND**
- Patient has squamous cell carcinoma or adenocarcinoma; **AND**
- Patient has unresectable, locally advanced, metastatic, or recurrent disease

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

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

§ Genomic Aberration/Mutational Driver Targeted Therapies [12] **(Note: *not all inclusive, refer to guidelines for appropriate use*)**				
Sensitizing *EGFR* mutation-positive tumors	*ALK* rearrangement-positive tumors	*ROS1* rearrangement-positive tumors	*BRAF* V600E-mutation positive tumors	*NTRK1/2/3* gene fusion positive tumors
– Afatinib – Erlotinib – Dacomitinib – Gefitinib – Osimertinib – Amivantamab *(exon-20 insertion)* – Mobocertinib *(exon-20 insertion)*	– Alectinib – Brigatinib – Ceritinib – Crizotinib – Lorlatinib	– Ceritinib – Crizotinib – Entrectinib – Lorlatinib	– Dabrafenib ± trametinib – Vemurafenib	– Larotrectinib – Entrectinib
PD-L1 tumor expression ≥ 1%	*MET* exon-14 skipping mutations	*RET* rearrangement-positive tumors	*KRAS G12C* mutation positive tumors	*ERBB2 (HER2)* mutation positive tumors
– Pembrolizumab – Atezolizumab – Nivolumab + ipilimumab – Cemiplimab – Tremelimumab + durvalumab	– Capmatinib – Crizotinib – Tepotinib	– Selpercatinib – Cabozantinib – Pralsetinib	– Sotorasib – Adagrasib	– Fam-trastuzumab deruxtecan-nxki – Ado-trastuzumab emtansine

IV. Renewal Criteria [1-6,8]

Coverage 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**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: gastrointestinal perforations and fistulae, surgical/wound healing complications, necrotizing

fasciitis, hemorrhage, 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.; **AND**

Adult CNS Cancers – symptom management (short-course therapy):

- Coverage may NOT be renewed

Adult CNS Cancers – Oligodendroglioma, Glioblastoma, or Astrocytoma (in combination with carmustine, lomustine, or temozolomide):

- *Refer to* Section *III for criteria*

Colorectal Cancer (after first-line bevacizumab-containing regimen):

- *Refer to Section III for criteria*

MPeM (combination therapy with atezolizumab):

- *Refer to Section III for criteria*

Non-Squamous Non-Small Cell Lung Cancer (maintenance therapy OR continuation therapy in combination with erlotinib):

- *Refer to Section III for criteria*

Ovarian Cancer (maintenance therapy):

- *Refer to Section III for criteria*

V. Dosage/Administration [1-4,7,8,13,18,30,36,37,39-48]

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	Administer 15 mg/kg intravenously every 3 weeks until disease progression or unacceptable toxicity.
Adult CNS Cancers	For disease treatment: –Administer 10 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity. For symptom management:

	–Administer 5 to 10 mg/kg intravenously every 2 weeks up to 12 weeks duration.
Pediatric CNS Cancers	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.
MPM	Administer 15 mg/kg intravenously every 3 weeks until disease progression or unacceptable toxicity.
MPeM	In combination with pemetrexed AND either cisplatin or carboplatin: –Administer 15 mg/kg intravenously every 3 weeks until disease progression or unacceptable toxicity. In combination with atezolizumab: –Administer 15 mg/kg intravenously every 3 weeks until disease progression or unacceptable toxicity.
Ovarian, Fallopian Tube, and Primary Peritoneal Cancer	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.
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

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

VII. References

1. Avastin [package insert]. South San Francisco, CA; Genentech, Inc.; September 2022. Accessed August 2023.
2. Mvasi [package insert]. Thousand Oaks, CA; Amgen, Inc.; February 2023. Accessed August 2023.
3. Zirabev [package insert]. New York, NY; Pfizer, Inc.; February 2023. Accessed August 2023.
4. Alymsys [package insert]. Bridgewater, NJ; Amneal Pharmaceuticals LLC; April 2022. Accessed August 2023.
5. Vegzelma [package insert]. Incheon, Republic of Korea; Celltrion, Inc.; September 2022. Accessed August 2023.
6. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) bevacizumab. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed August 2023.
7. Ceresoli GL, Zucali PA, Mencoboni M, et al. Phase II study of pemetrexed and carboplatin plus bevacizumab as first-line therapy in malignant pleural mesothelioma. Br J Cancer. 2013 Aug 6; 109(3): 552–558
8. Delishaj D, Ursino S, Pasqualetti F, et al. Bevacizumab for the Treatment of Radiation-Induced Cerebral Necrosis: A Systematic Review of the Literature. J Clin Med Res. 2017 Apr; 9(4): 273–280.
9. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. J Oncol Pract. 2018 Mar;14(3):e130-e136.
10. Hematology/Oncology Pharmacy Association (2019). *Intravenous Cancer Drug Waste Issue Brief*. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf
11. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. BMJ. 2016 Feb 29;352:i788.
12. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer 3.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed August 2023.
13. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer 2.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National

Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed August 2023.
14. Thatcher N, Goldschmidt JH, Thomas M, et al. Efficacy and safety of biosimilar ABP 215 compared with bevacizumab in patients with advanced nonsquamous non-small cell lung cancer (MAPLE): a randomized, double-blind, phase III study. Clin Cancer Res. 2019;25:2088-2095.
15. Reinmuth N, Bryl M, Bondarenko I, et al. PF-06439535 (a Bevacizumab Biosimilar) Compared with Reference Bevacizumab (Avastin®), Both Plus Paclitaxel and Carboplatin, as First-Line Treatment for Advanced Non-Squamous Non-Small-Cell Lung Cancer: A Randomized, Double-Blind Study. BioDrugs. 2019 Oct;33(5):555-570. Doi: 10.1007/s40259-019-00363-4.
16. Cheng AL, Qin S, Ikeda M, et al. LBA3-IMBrave150: Efficacy and safety results from a ph III study evaluating atezolizumab (atezo) + bevacizumab (bev) vs sorafenib (Sor) as first treatment (tx) for patients (pts) with unresectable hepatocellular carcinoma (HCC). Ann Oncol. 2019 Nov;30 Suppl 9:ix186-ix187.
17. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatocellular Carcinoma 1.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed August 2023.
18. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Small Bowel Adenocarcinoma 1.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed May 2023.
19. Hurwitz H, Fehrenbacher L, Novotny W, et al. Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer. N Engl J Med. 2004 Jun 3;350(23):2335-42.
20. Giantonio BJ, Catalano PJ, Meropol NJ, et al. Bevacizumab in combination with oxaliplatin, fluorouracil, and leucovorin (FOLFOX4) for previously treated metastatic colorectal cancer: results from the Eastern Cooperative Oncology Group Study E3200. J Clin Oncol. 2007;25(12):1539-1544.
21. Chen HX, Mooney M, Boron M, et al. Phase II multicenter trial of bevacizumab plus fluorouracil and leucovorin in patients with advanced refractory colorectal cancer: an NCI Treatment Referral Center Trial TRC-0301. J Clin Oncol. 2006;24(21):3354-3360. Doi:10.1200/JCO.2005.05.1573.
22. Bennouna J, Sastre J, Arnold D, et al. Continuation of bevacizumab after first progression in metastatic colorectal cancer (ML18147): a randomised phase 3 trial. Lancet Oncol. 2013 Jan;14(1):29-37.
23. de Gramont A, Van Cutsem E, Schmoll HJ, et al. Bevacizumab plus oxaliplatin-based chemotherapy as adjuvant treatment for colon cancer (AVANT): a phase 3 randomised controlled trial. Lancet Oncol. 2012;13(12):1225-1233. Doi:10.1016/S1470-2045(12)70509-0.

24. Allegra CJ, Yothers G, O'Connell MJ, et al. Phase III trial assessing bevacizumab in stages II and III carcinoma of the colon: results of NSABP protocol C-08. J Clin Oncol. 2011;29(1):11-16. Doi:10.1200/JCO.2010.30.0855.
25. Sandler A, Gray R, Perry MC, et al. Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer. N Engl J Med. 2006 Dec 14;355(24):2542-50.
26. Reck M, von Pawel J, Zatloukal P, et al. Phase III trial of cisplatin plus gemcitabine with either placebo or bevacizumab as first-line therapy for nonsquamous non-small-cell lung cancer: AVAil. J Clin Oncol. 2009 Mar 10;27(8):1227-34.
27. Wick W, Gorlia T, Bendszus M, et al. Lomustine and Bevacizumab in Progressive Glioblastoma. N Engl J Med 2017; 377:1954-1963.
28. Friedman HS, Prados MD, Wen PY, et al. Bevacizumab alone and in combination with irinotecan in recurrent glioblastoma. J Clin Oncol. 2009 Oct 1;27(28):4733-40.
29. Escudier B, Pluzanska A, Koralewski P, et al. Bevacizumab plus interferon alfa-2a for treatment of metastatic renal cell carcinoma: a randomised, double-blind phase III trial. Lancet. 2007;370(9605):2103-2111. Doi:10.1016/S0140-6736(07)61904-7.
30. Tewari KS, Sill MW, Penson RT, et al. Bevacizumab for advanced cervical cancer: final overall survival and adverse event analysis of a randomised, controlled, open-label, phase 3 trial (Gynecologic Oncology Group 240). Lancet. 2017;390(10103):1654-1663. Doi:10.1016/S0140-6736(17)31607-0.
31. Burger RA, Brady MF, Bookman MA, et al. Incorporation of bevacizumab in the primary treatment of ovarian cancer. N Engl J Med. 2011 Dec 29;365(26):2473-83.
32. Pujade-Lauraine E, Hilpert F, Weber B, et al. Bevacizumab Combined With Chemotherapy for Platinum-Resistant Recurrent Ovarian Cancer: The AURELIA Open-Label Randomized Phase III Trial. Journal of Clinical Oncology 2014 32:13, 1302-1308.
33. Aghajanian C, Blank SV, Goff BA, et al. OCEANS: a randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Clin Oncol. 2012;30(17):2039–2045.
34. Coleman RL, Brady MF, Herzog TJ, et al. Bevacizumab and paclitaxel-carboplatin chemotherapy and secondary cytoreduction in recurrent, platinum-sensitive ovarian cancer (NRG Oncology/Gynecologic Oncology Group study GOG-0213): a multicentre, open-label, randomised, phase 3 trial. Lancet Oncol. 2017;18(6):779–791.
35. Robert NJ, Diéras V, Glaspy J, et al. RIBBON-1: randomized, double-blind, placebo-controlled, phase III trial of chemotherapy with or without bevacizumab for first-line treatment of human epidermal growth factor receptor 2-negative, locally recurrent or metastatic breast cancer. J Clin Oncol. 2011 Apr 1;29(10):1252-60.
36. Agulnik M, Yarber JL, Okuno SH, et al. An open-label, multicenter, phase II study of bevacizumab for the treatment of angiosarcoma and epithelioid hemangioendotheliomas. Ann Oncol. 2013;24(1):257-263. Doi:10.1093/annonc/mds237.
37. Lorusso D, Ferrandina G, Colombo N, et al. Randomized phase II trial of carboplatin-paclitaxel (CP) compared to carboplatin-paclitaxel-bevacizumab (CP-B) in advanced (stage III-IV) or recurrent endometrial cancer: The MITO END-2 trial. Journal of Clinical Oncology 2015 33:15_suppl, 5502-5502.

38. Miller K, Wang M, Gralow J, et al. Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer. N Engl J Med. 2007 Dec 27;357(26):2666-76.
39. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Mesothelioma: Pleural 1.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed August 2023.
40. Zalcman G, Mazieres J, Margery J, et al; French Cooperative Thoracic Intergroup (IFCT). Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS): a randomised, controlled, open-label, phase 3 trial. Lancet. 2016 Apr 2;387(10026):1405-1414.
41. Park MS, Patel SR, Ludwig JA, et al. Activity of temozolomide and bevacizumab in the treatment of locally advanced, recurrent, and metastatic hemangiopericytoma and malignant solitary fibrous tumor. Cancer. 2011 Nov 1;117(21):4939-47. Doi: 10.1002/cncr.26098.
42. Rose PG, Ali S, Moslemi-Kebria M, et al. Paclitaxel, Carboplatin, and Bevacizumab in Advanced and Recurrent Endometrial Carcinoma. Int J Gynecol Cancer. 2017 Mar;27(3):452-458. Doi: 10.1097/IGC.0000000000000891.
43. Aghajanian C, Sill MW, Darcy KM, et al. Phase II trial of bevacizumab in recurrent or persistent endometrial cancer: a Gynecologic Oncology Group study. J Clin Oncol. 2011 Jun 1;29(16):2259-65. Doi: 10.1200/JCO.2010.32.6397.
44. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Mesothelioma: Peritoneal 2.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed August 2023.
45. Raghav KPS, Overman MJ, Liu S, et al. A phase II trial of atezolizumab and bevacizumab in patients with relapsed/refractory and unresectable malignant peritoneal mesothelioma. J Clin Oncol 2020;38:9013-9013.
46. Grill J, Massimino M, Bouffet E, et al. Phase II, Open-Label, Randomized, Multicenter Trial (HERBY) of Bevacizumab in Pediatric Patients With Newly Diagnosed High-Grade Glioma. J Clin Oncol 2018 Apr 1;36(10):951-958. Doi: 10.1200/JCO.2017.76.0611. Epub 2018 Feb 7.
47. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer Version 2.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed August 2023.
48. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Rectal Cancer Version 4.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc.

To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed August 2023.
49. Frumovitz M, Munsell MF, Burzawa JK, et al. Combination therapy with topotecan, paclitaxel, and bevacizumab improves progression-free survival in recurrent small cell neuroendocrine carcinoma of the cervix. Gynecol Oncol. 2017 Jan;144(1):46-50. Doi: 10.1016/j.ygyno.2016.10.040. Epub 2016 Nov 4. PMID: 27823771; PMCID: PMC5873577.
50. Prager GW, Taieb J, Fakih M, et al.; SUNLIGHT Investigators. Trifluridine-Tipiracil and Bevacizumab in Refractory Metastatic Colorectal Cancer. N Engl J Med. 2023 May 4;388(18):1657-1667. Doi: 10.1056/NEJMoa2214963. PMID: 37133585.
51. Bearz A, Talamini R, Rossoni G, et al. Re-challenge with pemetrexed in advanced mesothelioma: a multi-institutional experience. BMC Res Notes 2012;5:482
52. Nagao S, Kogiku A, Suzuki K, et al. A phase II study of the combination chemotherapy of bevacizumab and gemcitabine in women with platinum-resistant recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Ovarian Res 2020;13:14
53. National Government Services, Inc. Local Coverage Article: Billing and Coding: Bevacizumab and biosimilars (A52370). Centers for Medicare & Medicaid Services, Inc. Updated on 06/21/2023 with effective date 07/01/2023. Accessed August 2023.

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

ICD-10	ICD-10 Description
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
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

ICD-10	ICD-10 Description
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
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
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

ICD-10	ICD-10 Description
C57.22	Malignant neoplasm of left round ligament
C57.3	Malignant neoplasm of parametrium
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
C71.0	Malignant neoplasm of cerebrum, except lobes and ventricles
C71.1	Malignant neoplasm of frontal lobe
C71.2	Malignant neoplasm of temporal lobe
C71.3	Malignant neoplasm of parietal lobe
C71.4	Malignant neoplasm of occipital lobe
C71.5	Malignant neoplasm of cerebral ventricle
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
C72.0	Malignant neoplasm of spinal cord
C72.1	Malignant neoplasm of cauda equina
C72.9	Malignant neoplasm of central nervous system, unspecified
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
C83.39	Diffuse large B-cell lymphoma extranodal and solid organ sites

ICD-10	ICD-10 Description
C83.80	Other non-follicular lymphoma unspecified site
C83.89	Other non-follicular lymphoma extranodal and solid organ sites
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
D19.1	Benign neoplasm of mesothelial tissue of peritoneum
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
D48.1	Neoplasm of uncertain behavior of connective and other soft tissue
G93.6	Cerebral edema
I67.89	Other cerebrovascular disease
I67.9	Cerebrovascular disease, unspecified
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
Z85.841	Personal history of malignant neoplasm of brain
Z85.848	Personal history of malignant neoplasm of other parts of nervous tissue

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

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 Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and

compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA):

Jurisdiction(s): 6, K	**NCD/LCD Document (s):** A52370
https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a52370&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP	

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, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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

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- Qualified sign language interpreters
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200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
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ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 1.800.940.5049 (телетайп: 763.847.4013).

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ማስታወሻ: የሚናገሩት ቋንቋ አማርኛ ከሆነ የትርጉም እርዳታ ድርጅቶች፣ በነጻ ሊያግዝዎት ተዘጋጀተዋል፡ ወደ ሚከተለው ቁጥር ይደውሉ 1.800.940.5049 (መስማት ለተሳናቸው: 763.847.4013).

ဟသျှဉ်ဟသး– နမ့်ကတိ၊ ကညီ ကျိာ်အယိ, နမၤန့် ကျိာ်အတ်မၤစၢၤလ၊ တလၫ်ဘူဉ်လၫ်စ့၊ နီတမံၤဘဉ်သ့နှဉ်လီၤ. ကိး 1.800.940.5049 (TTY: 763.847.4013).

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PreferredOne Insurance Company ("PIC") complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. PIC does not exclude people or treat them differently because of race, color, national origin, age, disability, or sex.

PIC:
Provides free aids and services to people with disabilities to communicate effectively with us, such as:

- Qualified sign language interpreters
- Written information in other formats (large print, audio, accessible electronic formats, other formats)

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- Information written in other languages

If you need these services, contact a Grievance Specialist.

If you believe that PIC has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:

Grievance Specialist
PreferredOne Insurance Company
PO Box 59212
Minneapolis, MN 55459-0212
Phone: 1.800.940.5049 (TTY: 763.847.4013)
Fax: 763.847.4010
customerservice@preferredone.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, a Grievance Specialist is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

Language Assistance Services

ATTENTION: If you do not speak English, language assistance services, free of charge, are available to you. Call 1.800.940.5049 (TTY: 763.847.4013).

ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1.800.940.5049 (TTY: 763.847.4013).

LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1.800.940.5049 (TTY: 763.847.4013).

XIYYEEFFANNAA: Afaan dubbattu Oroomiffa, tajaajila gargaarsa afaanii, kanfaltiidhaan ala, ni argama. Bilbilaa 1.800.940.5049 (TTY: 763.847.4013).

CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1.800.940.5049 (TTY: 763.847.4013).

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