



Bevacizumab:

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

ONCOLOGY

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I. Length of Authorization ⁹

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, Avzivi:

- 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):

- CRC & Appendiceal Adenocarcinoma, CNS Cancers, RCC:
 - o 120 billable units per 14 days
- <u>Small Bowel Adenocarcinoma & Ampullary Adenocarcinoma</u>:
 - o 90 billable units per 14 days
- NSCLC, Cervical Cancer, HCC, Vaginal Cancer, Vulvar Cancer, & Mesotheliomas:
 - o 170 billable units per 21 days
- All other indications:
 - o 170 billable units per 14 days



III. Initial Approval Criteria 1-6

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 1-6

- 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 ‡ 7

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

Adult Central Nervous System (CNS) Cancers † ‡ Φ 1-7,9,28,29

- Used as single-agent short-course therapy for symptom management related to radiation necrosis, poorly controlled vasogenic edema, or mass effect; **AND**
 - o 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**
 - o Patient has a diagnosis of one of the following CNS cancers:



- IDH-mutant, 1p19q codeleted Oligodendroglioma (WHO Grade 3) ‡
- 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 † ‡ 1-7,31,50,61

- Patient has persistent, recurrent, or metastatic disease; AND
 - o 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^; AND
 - ➤ Used as first-line therapy; **OR**
 - > Used as subsequent therapy (if not previously used as first-line); **OR**
 - Used as a single agent as subsequent therapy

Colorectal Cancer (CRC) † ‡ 1-7,20-25,51

- Will not be used as part of adjuvant treatment; **AND**
 - Used in combination with intravenous fluorouracil-based chemotherapy as first- or secondline treatment for metastatic disease †; OR
 - 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; AND
 - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease;
 OR



[^] Bevacizumab may be continued as a maintenance therapy

- Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; AND
 - Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy; OR
- Used in combination with irinotecan as initial treatment for unresectable metastatic disease; AND
 - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease;
 AND
 - Patient received previous FOLFOX or CapeOX within the past 12 months; OR
- Used in combination irinotecan as subsequent therapy for advanced or metastatic disease;
 AND
 - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease;
 OR
 - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; AND
 - Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy; OR
- o 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 proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; OR
 - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation;
 AND
 - Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy; OR
- o Used as primary treatment for T3, N Any; T1-2, N1-2; T4, N Any 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; AND
 - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; OR



- Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; AND
 - Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy; OR
- Used if resection is contraindicated following neoadjuvant/definitive immunotherapy; AND
 - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease

Appendiceal Adenocarcinoma - Colon Cancer ‡ 7,48

- 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 proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease;
 OR
 - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; AND
 - Patient is not eligible 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 proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease;
 OR
 - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; AND
 - Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy; 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.)*;
 - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; OR



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

- Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation;
 AND
 - Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy

Endometrial Carcinoma (Uterine Neoplasms) ‡ 7,38

- Patient has recurrent disease; AND
 - o Used as a single agent; AND
 - Used as subsequent therapy for disease that has progressed on prior cytotoxic chemotherapy; OR
 - Used as continuation maintenance therapy following use in combination with carboplatin and paclitaxel; OR
 - o Used in combination with carboplatin and paclitaxel; AND
 - Used as first-line therapy (excluding use for isolated metastases); OR
 - Used as subsequent therapy

Hepatocellular Carcinoma (HCC) † ‡ Φ 1,7,17,18,55

- Used in combination with atezolizumab; AND
 - O Used as first-line therapy for unresectable or metastatic disease †; OR
 - Used as adjuvant therapy following resection or ablation; AND
 - Patient is at high risk of recurrence (defined as size > 5cm, > 3 tumors, macrovascular invasion or microvessel invasion on histology or grade 3/4 histology)

Peritoneal* Mesothelioma (PeM) ‡ 7,45,52

- Used as adjuvant therapy; **AND**
 - Used in combination with pemetrexed AND either cisplatin or carboplatin (if cisplatin ineligible); AND
 - o Patient has unicavitary disease with epithelioid histology; AND
 - Patient has surgical/pathologic high-risk features** and no neoadjuvant therapy was given; OR
- Used as first-line therapy; **AND**
 - Used in combination with pemetrexed AND either cisplatin or carboplatin (if cisplatin ineligible); AND
 - Patient has biphasic/sarcomatoid histology or bicavitary disease; OR
 - Patient has unicavitary disease with epithelioid histology; AND



^{*}Refer to NCCN Colon Cancer guidelines for regimens.

- Patient is medically inoperable and/or complete cytoreduction is not achievable (including high-risk features**); OR
- ➤ Patient has recurrent disease after prior cytoreductive surgery (CRS) + hyperthermic intraperitoneal (IP) chemotherapy (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 (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, retifanlimab, toripalimab, etc.)

Pleural* Mesothelioma (PM) ‡ 7,40,52

- Used as first-line therapy; **AND**
 - Used in combination with pemetrexed AND either cisplatin or carboplatin (if cisplatin ineligible); AND
 - Patient has clinical stage I-IIIA disease with epithelioid histology; OR
 - Patient has clinical stage IIIB or IV disease, sarcomatoid or biphasic histology, or medically inoperable 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

Non-Squamous Non-Small Cell Lung Cancer (NSCLC) † ‡ 1-7,13,15,16,26,27

 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



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

^{**} High-risk features include Ki-67>9%, nodal metastasis, high tumor burden (Peritoneal Cancer Index [PCI]>17), completeness of cytoreduction (CC) score>1, biphasic disease, or bicavitary disease.

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

- o 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:
 - Patients with a performance status (PS) 0-1 who have tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) and PD-L1 expression < 1%
 - PD-L1 expression positive (PD-L1 ≥ 1%) tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive)
 - Patients with a PS 0-1 who are positive for one of the following molecular biomarkers: EGFR exon 20, 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:
 - Pemetrexed AND either carboplatin or cisplatin in patients with contraindications¥ to PD-1 or PD-L1 inhibitors
 - Atezolizumab, carboplatin, and paclitaxel; **OR**
- o 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). Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, 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 rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

Ovarian, Fallopian Tube, and Primary Peritoneal Cancer † # \$\Phi\$ 1-7,14,32-35,53

- Patient has malignant stage II-IV sex cord-stromal tumors ‡; AND
 - o Used as a single agent for clinically relapsed disease; **OR**
- Patient has epithelial* ovarian, fallopian tube, or primary peritoneal cancer †; AND
 - o 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);
 - 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 oral cyclophosphamide and pembrolizumab; **OR**



- Used in combination with mirvetuximab soravtansine-gynx (in folate receptor-alpha expressing tumors); OR
- Used in combination with carboplatin AND either gemcitabine, paclitaxel or liposomal doxorubicin; 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 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 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 (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 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; **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

Pediatric Central Nervous System (CNS) Cancers ‡ 7,47,56-60

- Patient is ≤ 18 years of age; **AND**
- Patient has recurrent or progressive disease; AND
 - Patient has diffuse high-grade glioma (excluding oligodendroglioma, IDH-mutant and 1p/19q co-deleted or astrocytoma IDH-mutant), AND
 - Used as a single agent for palliation; **OR**
 - Patient has medulloblastoma; AND
 - Used as part of the TEMR regimen (temozolomide, irinotecan, bevacizumab); OR
 - Used as part of MEMMAT regimen (thalomide, celecoximb, fenofibrate, etoposide, cyclophosphamide, bevacizumab)

Renal Cell Carcinoma (RCC) † ‡ Φ 1-7,30

- Used in combination with interferon alfa for metastatic disease †; OR
- Patient has relapsed or metastatic disease with non-clear cell histology ‡; AND
 - o 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 ‡ 7,19

Patient has advanced or metastatic disease; AND



^{*}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).

• Used in combination with a fluoropyrimidine- (e.g., 5-fluorouracil/5-FU or capecitabine) based regimen

Soft Tissue Sarcoma ‡ 7,37,42

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

Vaginal Cancer ‡ 7,31,61

- Patient has recurrent or metastatic disease; AND
 - o Used in combination with paclitaxel AND either cisplatin, carboplatin, or topotecan; AND
 - Used as first-line therapy; OR
 - Used as subsequent therapy (if not previously used as first-line); 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 test ❖; AND
 - > Used as first-line therapy; **OR**
 - ➤ Used as subsequent therapy (if not previously used as first-line); **OR**
 - o Used as a single agent; AND
 - Used as subsequent therapy

Vulvar Cancer ‡ 7,31

- Used in combination with paclitaxel and cisplatin; AND
- Patient has advanced, recurrent, or metastatic disease; AND
 - o Used as first-line therapy; **OR**
 - Used as subsequent therapy (if not previously used)
- 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			
(Note: not all inclusive, refer to guidelines for appropriate use)			
EGFR exon 19 deletion or exon 21 L858R tumors	EGFR S768I, L861Q, and/or G719X mutation positive tumors	EGFR exon 20 insertion mutation positive tumors	NTRK1/2/3 gene fusion positive tumors
– Afatinib	- Afatinib	– Amivantamab	Larotrectinib
– Erlotinib	Erlotinib		— Entrectinib
Dacomitinib	Dacomitinib		
– Gefitinib	– Gefitinib		
Osimertinib	Osimertinib		
Amivantamab	Amivantamab		
ALK rearrangement-positive	ROS1 rearrangement-positive	BRAF V600E-mutation positive	ERBB2 (HER2) mutation
tumors	tumors	tumors	positive tumors

BEVACIZUMAB

(AVASTIN®; MVASI®; ZIRABEV®; ALYMSYS®; VEGZELMA®; AVZIVI®)



AlectinibBrigatinib	CeritinibCrizotinib	Dabrafenib ± trametinibEncorafenib + binimetinib	– Fam-trastuzumab deruxtecan-nxki
Ceritinib	Entrectinib	Vemurafenib	 Ado-trastuzumab emtansine
Crizotinib	Lorlatinib		
Lorlatinib	Repotrectinib		
PD-L1 tumor	MET exon-14 skipping mutations	RET rearrangement-positive	KRAS G12C mutation
expression ≥ 1%		tumors	positive tumors
 Pembrolizumab 	Capmatinib	Selpercatinib	Sotorasib
 Atezolizumab 	- Crizotinib	 Cabozantinib 	Adagrasib
 Nivolumab + ipilimumab 	- Tepotinib	Pralsetinib	
Cemiplimab			
Tremelimumab +			
durvalumab			

IV. Renewal Criteria 1-7,9

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 (in combination with carmustine, lomustine, or temozolomide):

Refer to Section III for criteria

Cervical Cancer (maintenance therapy):

Refer to Section III for criteria

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

Refer to Section III for criteria

Endometrial Carcinoma (Uterine Neoplasms) (maintenance therapy)

Refer to Section III for criteria

PeM* (combination therapy with atezolizumab):

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without approval.





- Refer to Section III for criteria
- * Includes use for pericardial mesothelioma and tunica vaginalis testis mesothelioma.

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

• Refer to Section III for criteria

Ovarian Fallopian Tube, and Primary Peritoneal Cancer (maintenance therapy):

• Refer to Section III for criteria

V. Dosage/Administration ^{1-6,8,9,14,19,31,37,38,40-49,54-61}

Indication	Dose
CRC & Appendiceal Adenocarcinoma	Administer 5 to 10 mg/kg intravenously every 2 weeks <u>OR</u> 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, & 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 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 OR 7.5 mg/kg intravenously every 3 weeks up to 12 weeks.
Pediatric CNS Cancers & 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 <u>OR</u> 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

BEVACIZUMAB
(AVASTIN®; MVASI®; ZIRABEV®; ALYMSYS®; VEGZELMA®;

AVZIVI®)

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- 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
- J9999 Not otherwise classified, antineoplastic drugs (Avzivi 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

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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

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ICD-10	ICD-10 Description		
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		
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		

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ICD-10	ICD-10 Description	
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	
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	

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ICD-10	ICD-10 Description	
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	
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	

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ICD-10	ICD-10 Description		
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		
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		
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		
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		

(AVASTIN®; MVASI®; ZIRABEV®; ALYMSYS®; VEGZELMA®;







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	Contractor
	Document (s)	
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		



Nondiscrimination & Language Access Policy



Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:

Provides people with disabilities reasonable modifications and free appropriate auxiliary aids and services to communicate effectively with us, such as:

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

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If you need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If you believe that Aspirus Health Plan, Inc. 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:

Nondiscrimination Grievance Coordinator

Aspirus Health Plan, Inc.

PO Box 1890

Southampton, PA 18966-9998

Phone: 1-866-631-5404 (TTY: 711)

Fax: 763-847-4010

Email: customerservice@aspirushealthplan.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Nondiscrimination Grievance Coordinator 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. This notice is available at Aspirus Health Plan, Inc.'s website: https://aspirushealthplan.com/webdocs/70021-AHP-NonDiscrim_Lang-Assist-Notice.pdf.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë. Telefononi në 1-800-332-6501 (TTY: 711).

Arabic تنبيه : إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً اتصل بن اعلى رقم الهاتف6501-332-800-1(رقم هاتف الصم والبك : 711)

French: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

Hindi: _यान द _: य _द आप िहंदी बोलते ह _तो आपके िलए मु _त म _ भाषा सहायता सेवाएं उपल _ध ह _11-800-332-6501 (TTY: 711) पर कॉल कर _ I

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.1-800-332-6501 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer1-800-332-6501 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 1-800-332-6501 (телетайп: 711)

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al1-800-332-6501 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1-800-332-6501 (TTY: 711).

Traditional Chinese: 注意: 如果您使用繁體中文, 您可以免費獲得語言援助服務。請 致電 1-800-332-6501 (TTY: 711)

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1-800-332-6501 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັຽຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-800-332-6501 (TTY: 711).